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# 鑄造業勞工暴露游離二氧化矽之肺功能及氧化傷害研究

# The lung effect and oxidative damage of free silica exposure among foundry workers

林洺秀
Ming-Hsiu Lin

指導教授：劉紹興博士 張靜文博士
Advisor: Saou-Hsing Liou, Ph.D.
Ching-Wen Chang, Ph.D.

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# 國立臺灣大學博士學位論文
# 口試委員會審定書

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本論文係林洺秀君( 學號 F91844016 )在國立臺灣大學環境衛生研究所完成之博士學位論文，於民國 99 年 12 月 20 日承下列考試委員審查通過及口試及格，特此證明

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張靜文 （簽名）

劉紹樂 （指導教授）

鄭尊仁 （指導教授）

孟明哲

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# 誌　謝

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洺秀謹致

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# 摘　要

由於勞工長期暴露於含游離二氧化矽之粉塵作業環境中，易導致矽肺症，日後亦成為肺癌之高危險群。而以往文獻幾乎多著墨於動物實驗研究或人類流行病學調查，而有關實際進行職場暴露改善與人體健康效應間之量測，則少有研究探討。本研究將以鑄造業勞工為對象，以尿中之 8-羥基去氧鳥糞核苷(8-OHdG)濃度作為氧化傷害指標；針對以實際工程改善介入工作現場，探討肺功能及 8-OHdG 等生物指標之變化，以期達到早期預防矽肺症及肺癌之產生。

本研究收集 A、B、C 鑄造廠廠研究對象共 74 人，進行胸部 X 光、肺功能、血液常規、生化、氧化傷害等檢查，了解肺功能與飲食攝取、氧化傷害、抗氧化能力指標、職場暴露、身體質量指數(BMI)等相關性。結果發現，肺功能中第一秒用力呼氣容量（FEV1）、FEV1%pred、一秒量率(FEV1/FVC%)與職場粉塵累積暴露濃度、BMI 等趨勢分佈皆達顯著負相關。另外，針對 A 廠進行工廠作業環境改善及追蹤該廠作業員工之肺功能及 8-OHdG 濃度，在作業環境改善後三個月再次進行一次肺功能及尿中 8-OHdG 等檢查。結果發現， A 鑄造廠在環境改善後可呼吸粉塵濃度及游離二氧化矽有減少之現象，針對同樣的研究對象進行肺功能指標重複施測，發現其肺功能指標 FEV1、用力肺容量(FVC)、FEV1%pred、FVC%pred 在作業環境改善後有明顯的增加，並達統計顯著差異。在針對 B 鑄造廠勞工 DNA 損傷、免疫毒性及職場暴露之分析方面，在校正一些干擾因子(如年齡、籍貫、教育程度、吸菸情形及維他命 E 使用情形等)後，發現累積暴露量與 DNA 傷害四參數，頭尾比例、尾部長度、尾部動量、Oliver 尾矩皆具有統計上顯著意義。至於勞工細胞激素分佈方面，將年齡、籍貫、吸菸情形、BMI 及是否罹患矽肺症等因子納入複迴歸分析模式中，可以了解白介素－2(IL-2)及白介素－10(IL-10)與是否罹患矽肺症具有統計上之顯著意義；即罹患矽肺症(含 1/0 以上)之勞工較未罹患矽肺症之勞工有較高 IL-2、IL-10。

由本研究中勞工職場游離二氧化矽之累積暴露與健康效應方面，顯示職場暴露導致該族群之肺功能下降、DNA 損傷；而藉由水霧工程之現場輔導，肺功能在作業環境改善後有明顯的增加。因此建議即時工程介入改善作業環境現場對於防治鑄造業勞工矽肺症是必要的。

關鍵詞：游離二氧化矽、鑄造業勞工、8-羥基去氧鳥糞核苷、DNA 傷害、細胞激素

# Abstract

Laborer workers are exposed to free silica long-term and lead to an increased risk of silicosis and lung cancer. Epidemiological and animal studies support that, then less research resulting from an engineering intervention to assess the health effect. The primary aim of this study was to evaluate changes in lung function and oxidative damage markers following the introduction of an engineering control intervention , whilst urinary 8-hydroxy-deoxyguanosine (8-OHdG) was used as a measure of oxidative DNA damage.

My study population was 74 male from 3 foundries in Taiwan. All subjects were carried on such inspections as chest X-rays, lung function, blood routine, oxidative damage,etc, in order to discuss the effects of dust exposure and BMI on foundry workers' lung function and to determine whether the intake of dietary vitamins has any significant impact in improving lung function and anti-oxidant plasma activity. Our findings revealed that the lung function, FEV1, FEV1%pred and FEV1/FVC% of foundry workers is negatively affected by having a higher BMI and by exposure to dust. In addition, I studied one of 3 foundries before, and three months after, improvements to air exhaust control. Initial baseline biomarker measurements were taken of lung function and urinary 8-OHdG in all of the workers, with follow up measurements taken three months after the engineering control was put in place. Compared to initial baseline, significant improvements were found in lung function (FVC, FEV1, FVC%pred and FEV1%pred) amongst the workers after the engineering intervention to reduce the silica level. I estimated DNA damage by comet assay for another planet, after confounders were adjusted, A significant increase in L/H, TL, ETM, OTM of DNA damage with cumulative silica exposure. From the result of cytokines showed that the significant higher concentration of IL-2 and IL-10 in

silicosis subjects (equal and more than ILO 1/0) than health workers.

These findings indicate that significant improvements in lung function among a small group of foundry workers following the implementation of an engineering intervention that effectively reduced the levels of respirable silica dust. These results suggest that engineering controls aimed at reducing occupational exposure to silica represent an effective approach that may have immediate benefits to workers.

Keyword: free silica, foundry worker, 8-hydroxy-deoxyguanosine, DNA damage, cytokines

# 目錄

# 圖目錄

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# 第一章 緒論

## 第一節 研究背景

職業上暴露到可呼吸性游離二氧化矽是需要受到重視的，因含游離二氧化矽的粉塵沉積於肺泡中會造成肺部纖維化而產生『矽肺症』，游離二氧化矽的危害早在 15、16 世紀被發現，當時以礦工、採石工…等為主，由於這些暴露族群為中下階級，所以並未受到關注(DHHS, 1995)，直到 1935 年，美國 Gaulay Bridge 地下隧道挖掘工程，發現 3000 名參與的勞工，有 700 位罹患急性矽肺症而死亡，並且有超過 1500 位罹患矽肺症或肺結核，因此才引起國際上關注(Chemiak, 1986; Goldsmith, 1997)。

另根據台灣地區勞工保險職業病給付資料統計，塵肺症一直佔所有職業病給付大宗（2006~2009 統計，塵肺症佔 6.4% ）。近年來，肌肉骨骼傷害引起之下背痛及手背頸肩疾病，該職業病給付次數已遠超越塵肺症；但其皆為較輕微之職業傷病，藉由人體工學設計或調離工作現場，勞工傷害可立即改善。不若塵肺症引起之職業病幾乎皆為職業殘廢，即使離開工作現場，勞工其肺部功能仍持續惡化。以 2009 年之職業病給付人次統計而言，給付塵肺症及矽肺症之個案數為 21 件，佔所有職業病給付次數之 4.4% ，但佔所有職業病失能給付之 27.5%（勞保統計年報，2010）。而勞工罹患塵肺症的主因係因勞工長期吸入不溶性粉塵而沈積於肺部所致，其中尤以游離二氧化矽為鉅，其會於肺內形成細小而規則的纖維性小結，矽肺小結會融合而成為進行性大塊纖維化，引發呼吸困難甚至死亡。不僅國內勞工罹患矽肺症比例高，國外亦是如此。根據 David(1998) 指出美國每年約有 2 百萬勞工暴露於游離二氧化矽的工作環境中，而平均每百萬工人中約有 59,000 名工人日後可能會罹患矽肺症；Daniel (1999)亦指出美國每年仍有超過 250 位勞工死於矽肺症。

依據所暴露空氣中游離二氧化矽之濃度不同，矽肺症主要可分為三種形式

(DHHS,1995)：Ⅰ慢性矽肺症，暴露於較低游離二氧化矽濃度之作業環境下，通常暴露十年後才會發生症狀；Ⅱ累積型矽肺症，暴露於較高游離二氧化矽濃度之作業環境下，通常暴露五至十年間才會發生症狀；Ⅲ急性矽肺症，暴露於極高游離二氧化矽濃度之作業環境下，通常暴露數週至五年內會發生症狀。矽肺症雖然是一種不可逆的病變，而且目前也並沒一種有效的治療方法，但是對於保護勞工立場，仍應藉著早期病症的發現並且立即停止暴露以達到預防矽肺症的效果。

空氣中懸浮微粒之粒徑尺寸大小不同對人體健康危害影響不同。若在相同質量下，較小粒徑的微粒，其總表面積相較於較大微粒大，故其微粒表面可攜帶較多的有毒物質及活性氧化物，因此造成肺泡傷害也較粗微粒大。甚至微粒所攜帶的致癌物可經由微血管循環輸送至身體其他地方而引起全身性發炎(Nightingale et al.,2000)。而依吸入的懸浮微粒尺寸大小，可受微粒的沈降部位、肺清除能力、肺部沈降區域及呼吸型態等因素共同決定。根據 ACGIH 之定義，吸入性（inhalable）粉塵為氣動直徑 $D_{50}$ 為 100 $\mu$m 之粉塵，胸腔性（thoracic）粉塵為氣動直徑 $D_{50}$ 為 10 $\mu$m 之粉塵，呼吸性（respirable）粉塵為氣動直徑 $D_{50}$ 為 4 $\mu$m 之粉塵，因此本研究之勞工暴露評估主要係探討可呼吸性粉塵中之游離二氧化矽危害。Gulumian（1999）指出當勞工暴露於含游離二氧化矽粉塵至肺癌產生過程中，經歷巨噬細胞之活化、肺部發炎、肺部纖維化等。而游離二氧化矽的暴露會造成矽肺病、自體免疫的疾病以及肺癌；而發炎反應似乎是暴露二氧化矽後相當常見的之初步反應。研究也證實二氧化矽之水溶液會產生 $H_2O_2$, HO・,O・等自由基(Konecny, 2001)，其可能對人體因此造成氧化傷害。而當暴露一環境中致癌物後至癌症產生前，其可能歷經內在劑量、生物有效劑量、早期生物效應、組織結構改變、癌症症狀產生(Ross et al.,1992)，而一般法令，如勞工健康保護規則中規範粉塵作業場所之勞工定期健康檢查，其胸部 X 光判讀矽肺症之結果已屬於後期的組織結構改變，常為時已晚。

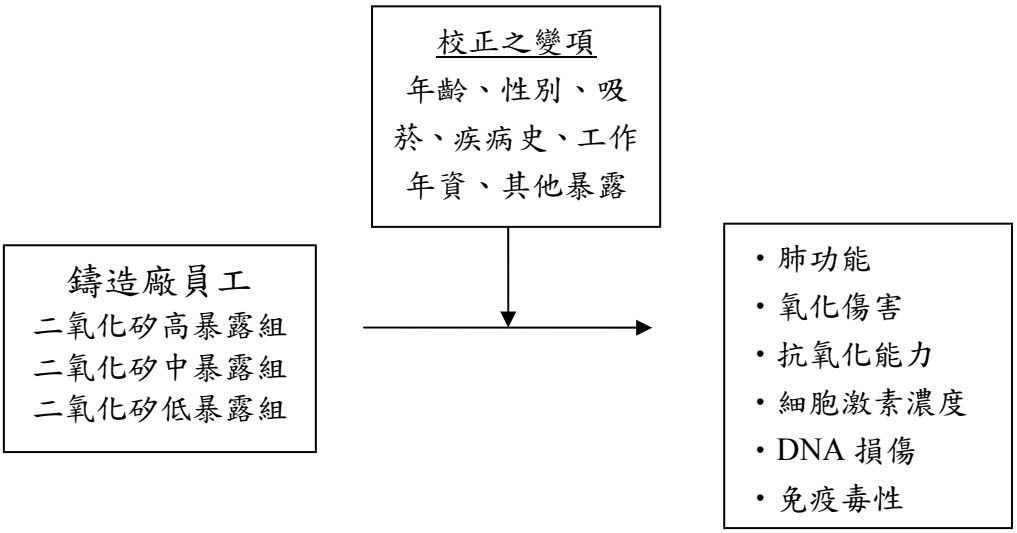
而鑄造業為機械工業之母，最早期應用在各種武器的製造，至今則使用在日

常用品與機械零件，在台灣鋼鐵鑄造業總共約 1240 家，員工約 16729 位。鑄造工廠中所使用的鑄砂主要的成分為二氧化矽，因此鑄造廠工作者暴露到二氧化矽的機會很高，在國內外都有針對鑄造業的一些研究發現，鑄造業的員工有較高的肺部疾病盛行率。因此本研究將針對鑄造業勞工，進行其肺功能、胸部 X 光、氧化傷害指標、免疫毒性等各項健康檢查，探討其暴露於游離二氧化矽下導致之健康危害。

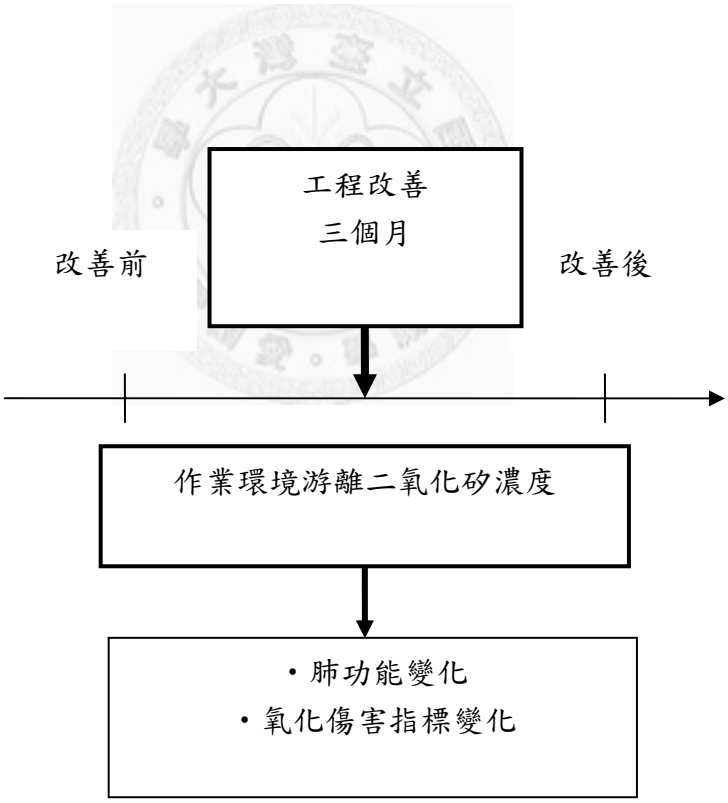
## 第二節 研究目的

本研究以鑄造業勞工為對象，進行橫斷性研究及縱斷性追蹤。橫斷性研究方面：了解該族群其肺功能與飲食攝取、氧化傷害、抗氧化能力指標、細胞激素濃度、DNA 損傷、免疫毒性、BMI、職場暴露等相關性。縱斷性追蹤方面：以實際工程改善介入工作現場過程中，針對改善工廠之勞工探討各生物指標之變化，以期早期協助勞工的工作現場，達到預防矽肺症及肺癌之產生，以做為粉塵作業勞工健康危害研究的參考。本研究架構如下：

一、 橫斷性研究




二、 縱斷性研究



# 第二章 文獻探討

## 第一節 游離二氧化矽

二氧化矽為矽酸鹽的一種，主要分為『結晶型』與『非結晶型』兩種形式。結晶型游離二氧化矽係指矽原子共用四個氧原子相互結合成三度空間立體架構，其在地球上分佈相當廣泛；其同質異形體計有石英、鱗矽石、方矽石、斜矽石、重矽石。而在自然環境下存有石英、鱗矽石、方矽石，且大多以石英方式存在。各種游離二氧化矽會因為不同的溫度、壓力條件而相互轉換。一大氣壓下，石英穩定存在溫度低於 870℃的環境下；鱗矽石為 870℃到 470℃；方矽石則在 1470℃到其融點 1710℃之間。而不同之結晶構造致使其對生物細胞之作用亦不相同，由老鼠實驗之支氣管沖洗液得知暴露於各種不同二氧化矽晶形體時，造成之危害程度不相同（Warheit et al.,1995）；George et al.（1995）指出各游離二氧化矽之晶形不同，其對生物體之危害亦有差異。因此各國對於勞工暴露於石英、鱗矽石、方矽石之規範亦不相同（ACGIH,2006）；如美國職業安全衛生署(OSHA)對鱗矽石、方矽石之容許濃度規範值為石英之一半。而鑑於游離二氧化矽之危害，國際癌症研究署(IARC)依據各種粉塵作業勞工之流行病學證據，於 1997 年將游離二氧化矽之石英、方矽石歸類於人類致癌物(GROUP 1)，鱗矽石歸類於疑似人類致癌物(GROUP 2A)。但我國法令僅規範含游離二氧化矽之粉塵，並未再細分石英、鱗矽石、方矽石不同結晶體之差異。依據勞工作業環境空氣中有害物容許濃度標準之規定，我國將粉塵分為四種，第一種粉塵為含游離二氧化矽 10 %以上之礦物性粉塵，第二種粉塵為含游離二氧化矽未滿 10 %之粉塵，第三種粉塵為石綿纖維，第四種粉塵為厭惡性粉塵。本研究之研究對象，鑄造業勞工之作業環境暴露範圍係隸屬於第一種及第二種粉塵。

## 第二節 游離二氧化矽之流行病學研究

早在 1938 年國外學者 Turner 和 Grace 研究已說明在英國雪費爾鑄造工人一些呼吸道癌症（例如：肺癌）死亡率過高，在同時間，流行病學證據說明鑄造工作與其後的呼吸道疾病（惡性或非惡性）有正相關(Turner et al., 1938)。相關文獻指出鑄造廠勞工暴露時間在 20 年以內，其矽肺症發生率為 1.5%，但是超過 20 年將會暴增到 53%，且呼吸道異常的盛行率也隨時間越長而升高；而暴露到游離二氧化矽，罹患所有癌症的相對危險性為 1.3~1.5(Landrigan et al., 1986)。

為了解游離二氧化矽對勞工之危害，Murray（1995）針對安大略省採礦、石作、鑄造等暴露於游離二氧化矽之工人進行世代及個案對照組之調查，由胸部 X-光片發現暴露於游離二氧化矽之作業場所將使工人罹患肺癌之風險增加；而工作暴露三十年之矽肺症罹患風險為暴露二十年者之 1.6 倍。Franco (1995)由義大利 San Martino 醫院之肺部死亡率資料統計得知矽肺症之 SMR 值為 1.89，矽肺肺結核症之 SMR 值為 27，肺癌之 SMR 值為 3.5 等。Nicholas(1998)針對澳洲金礦工人矽肺症、肺癌進行調查，發現暴露於游離二氧化矽使矽肺症及隨後伴隨之肺癌罹患風險增高，但若無罹患矽肺症者，並無證據顯示其罹患肺癌之機率增加。

過去研究說明游離二氧化矽的暴露可能造成矽肺症、自體免疫反應疾病及肺癌的發生，Hnizdo and Sluis-Cremer (1993)及 Rice and Stayner (1995)針對 2,235 位南非的金礦工進行調查，發覺若暴露在可呼吸性游離二氧化矽平均濃度 0.05mg/$m^3$ 環境下，則其矽肺症盛行率為 13/100（≧ILO 1/1）；而若暴露之平均濃度 0.10mg/$m^3$ 環境下，則其矽肺症盛行率為 70/100（≧ILO 1/1）。一些相關之流行病學研究，包括：Hughes et al. (1995)進行 2,342 美國矽藻土礦場勞工調查、Kreiss and Zhen (1996)以 100 位美國礦場勞工當暴露組及 34 位社區區民當對照組、Muir(1989)針對加拿大 2,109 位金礦及釉礦勞工進行調查、Ng and Chan (1994)的 338 位香港花崗岩礦工、Steenland and Brown （1995）進行美國科羅拉多 3,330 位的金屬礦工，均顯示職業性的游離二氧化矽暴露會導致矽肺症產生，

甚至在暴露停止後慢性的矽肺症仍會繼續發展及惡化。而且該流行病學研究提供證據說明使用累積性暴露資料來瞭解游離二氧化矽暴露反應與矽肺症之關係。而根據美國、英國、中國、丹麥、義大利、芬蘭等各地有關矽藻土礦場、陶瓷作業、金礦礦場、耐火磚作業等粉塵作業勞工之流行病學調查，以累積暴露數據為基礎的暴露-反應模式能夠預測暴露一段時間的游離二氧化矽微粒其罹患矽肺症之危險性，也有些以暴露時間等方式來證實游離二氧化矽與矽肺症的暴露-反應關係(如表 1)(Hnizdo and Sluis-Cremer 1993; Muir et al. 1989a,b; Muir 1991; Goldsmith, 1994a, 1998; Rice et al., 1995; Seaton, 1995; Steenland et al., 1995a; WHO., 1986)。而 IARC 亦依此相關職業暴露等流行病學研究，判斷游離二氧化矽的暴露可導致肺癌的發生，將游離二氧化矽之石英、方矽石歸類於人類致癌物(GROUP 1)，鱗矽石歸類於疑似人類致癌物(GROUP 2A)。

Amandus et al.（1995）針對美國北卡羅納州粉塵作業罹患矽肺症之 741 位勞工進行死亡率調查；在校正年齡及抽菸等因素後，發現其相對危險性(RR)值為 3.9。Kyle 和 Wayne 的研究結果說明在 1974 到 1995 年所收集到暴露游離二氧化矽的個案，矽肺症/塵肺症的標準化死亡率為 18.2（95%信賴區間＝10.6,29.1），而肺癌的標準化死亡率是 1.60（95%信賴區間＝1.31,1.93）(Kyle et al., 2001)。一橫斷性研究顯示在南非的金礦工人有高肺結核盛行率，結核病史的盛行率為 19.4%，且與粉塵及游離二氧化矽暴露有達到統計上相關(teWaterNaude et al., 2006)。

在鑄造廠與陶瓷工廠之調查結果顯示，長期暴露到游離二氧化矽也可能會對人體免疫系統有害(Basaran et al., 2002)，暴露游離二氧化矽後初步之發炎反應，應是與細胞型和體液型免疫功能改變有關(Shaklin et al., 1998; SSDC., 1988)。

在國內有關鑄造工廠的研究，如在 1985 年毛等人發現一間 179 位員工的鑄造工廠，其依照工作區域的不同，可呼吸性的粉末濃度變異(0.3-112mg/$m^3$)非常大，

而有20%的員工被發現有肺部功能異常的情形;在台南醫院有327位來自10間鑄造廠的員工，發現 9.73%的人有肺部功能異常的情形，以及 2.7%有矽肺症的發生；1999 年，Kuo et al.針對中台灣的鑄造廠做一個橫斷性的研究發現，與行政人員比較，熔爐工人得塵肺症的危險性是行政人員 8.98 倍；鑄件處理工人則為 6.77 倍，兩者皆有統計上顯著；造模工人則為5.41倍，但未達統計上顯著(Kuo et al., 1999)。在1990年林等人調查台灣16間鑄造廠共291位員工發現有12.7%的員工肺部功能異常且有6.9%的員工罹患矽肺症；然而在國外，在1987年Myers等人研究也發現在南非的鑄造工人中有 10.3%的工人診斷為塵肺症(Myers et al., 1987)。Rosenman et al.(1996)針對 1,072 美國鑄造廠員工進行調查，依據平均40 年工作時間且控制抽菸、種族等，得知暴露在可呼吸性游離二氧化矽平均濃度0.05mg/$m^3$環境下，則其矽肺症（ILO ≧1/0）盛行率為2/100；而若暴露之平均濃度0.10mg/$m^3$環境下，則其矽肺症盛行率為3/100。

## 第三節 游離二氧化矽與氧化傷害

自由基(free radical)是指含有一個或多個不成對電子而獨立存在之原子或分子，由於含有不成對電子所以大部分的自由基處於極不穩定狀態，易與鄰近分子產生反應而造成潛在性危害，因此研究學者認為自由基與疾病、老化及癌症有密切關係。而氧化壓力的產生即因自由基與活性氧化物(ROS, Reactive Oxygen Species)產生過多、抗氧化物防禦機轉缺失及游離態過渡金屬增加（Kelly, 2003）。自由基或活性氧化物之來源包含內因性及外因性，內因性主要來自於粒線體中呼吸作用的副反應；外因性可因環境的暴露，例如空氣污染、抽菸等(Block et al., 2002; Kelly, 2003)。

游離二氧化矽可轉變成ROS，Shi et al.利用電子自旋法(ESR)測得空氣懸浮的每公克二氧化矽微粒在 30 分鐘內可以產生 1018 的自由基；然而也發現新鮮(Freshly)的二氧化矽產生自由基的量比年老(Aged)的二氧化矽多，也就是說二氧

化矽存在於空氣中的時間越長，所產生的自由基濃度愈低，測得的 ESR 強度會隨著二氧化矽存在時間增加而減少(Shi et al., 1998)。另外 Konecny et al.(2001)也提出，空氣中二氧化矽之水溶液會產生 $H_2O_2$、HO・、O・等自由基，證實二氧化矽與活性氧化物之關係。而氧化壓力造成基因毒性影響而增加細胞凋亡、微小核(micronuclei)形成及染色體缺失(Bresgen et al., 2003)，在體內，游離二氧化矽的肺部反應為導致矽肺症與肺部致癌，當外在的游離二氧化矽進入人體後，其可能對 DNA 造成傷害而致使肺部致癌。一般 DNA 傷害包含 DNA 鍵結物（生物有效劑量指標）以及染色體變異、姊妹染色體交換(sister chromatid exchange)、微小核和 DNA 股斷裂（早期生物效應指標）的產生。

在關於游離二氧化矽的研究文獻中指出，細胞毒性與不同的形狀與大小之游離二氧化矽以及細胞所暴露表面之程度有關(Fubini & Hubbard, 2003)。

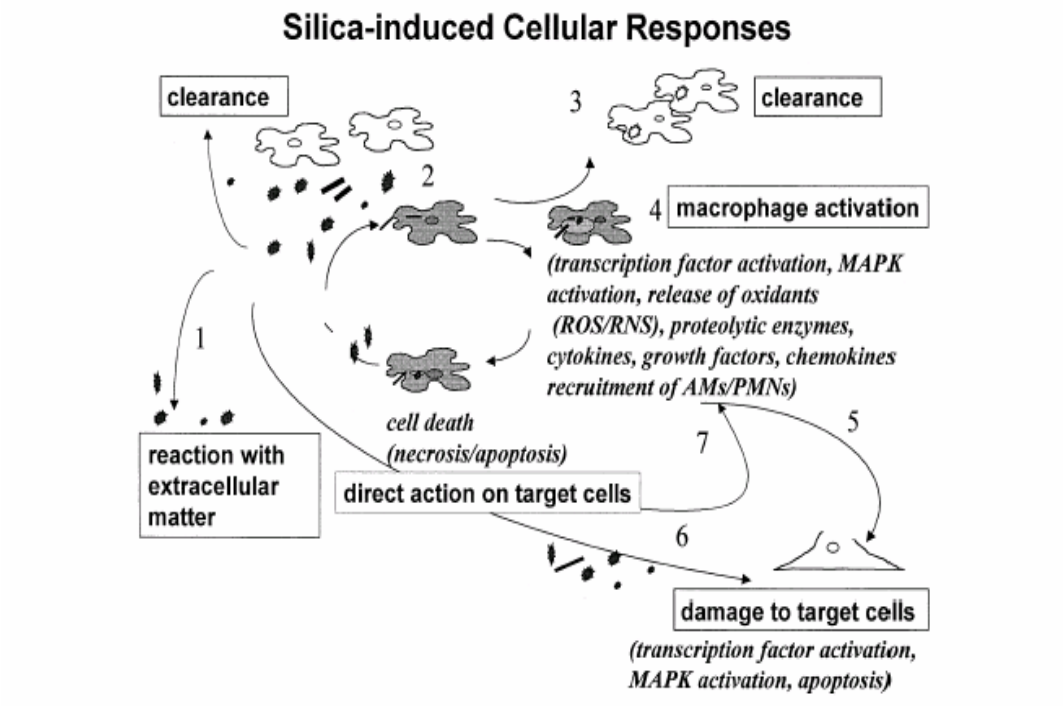



Fig. 1. Silica-induced cellular responses. (1) Interaction with extracellular matter; (2) phagocytosis by alveolar macrophages (AM); (3) clearance; (4) macrophage activation and death; (5) response by target cells to AM products; (6) direct action of the particle on target cells; (7) generation of additional ROS/RNS species.

圖 1　游離二氧化矽導致肺部細胞之反應

Fubini 及 Hubbard 以圖 1 說明暴露二氧化矽後可能引發之細胞反應，首先二氧化矽會於肺泡腔與細胞外之物質反應（步驟一），誘發肺部巨噬細胞前來進行

清除之工作（步驟二），清除之工作可能成功（步驟三）或失敗（步驟四），若是清除失利，巨噬細胞會啟動轉錄因子並且釋放 ROS、活性氮化物(RNS, Reactive Nitrogen Species)、細胞激素、生長因子等最後造成細胞的凋零或死亡以及二氧化矽微粒之釋出；這樣一連串的吞噬、再吞噬將驅使中性白血球、淋巴球，慢性發炎反應因而產生，支氣管或肺部上皮細胞等目標細胞也會受肺部巨噬細胞的產物以及細胞外之二氧化矽微粒所影響導致巨噬細胞之啟動或細胞死亡。

Du 和 Wang 則探討(2003)二氧化矽可能導致健康的效應機轉，暴露二氧化矽後之老鼠，支氣管肺部之灌洗細胞發現會增加氧氣之消耗，二氧化矽進入到肺泡時，會激發肺部巨噬細胞與表皮細胞形成細胞激素(cytokine)，因而會驅使發炎細胞的產生加強發炎的反應( Interluin-6, IL-6; tumor necrosis factor, TNF-$\alpha$)。巨噬細胞對懸浮微粒會進行胞噬作用，並且產生 ROS 與 RNS。ROS 與 RNS 會對附近之表皮與內皮細胞造成損傷，最後也會致使凝血蛋白如 fibrinogen 增加並影響血液的黏稠度(Ulrich et al., 2002) 。另外懸浮微粒上帶有自由基則直接會活化內生性介質，這些介質如細胞激素、腫瘤壞死因子(TNF)、白血球間素-1(IL-1)、血小板致活因子（PAF）等；這些介質並會進一步誘發宿主產生過量的一氧化氮。

Zhang et al.發現吸入游離二氧化矽之大鼠其肺部之第二型肺泡上皮細胞之氧化岐化酶(superoxide dismutase, SOD)會明顯的增加，麩胱甘肽過氧去氫 mRNA 酶氫會明顯的增加(glutathione），暴露組其肺部組織 GSH 則較對照組有明顯降低的趨勢(Zhang et al., 1999)。另游離二氧化矽亦會增加肺泡中過氧化氫與超氧陰離子的含量(Zhang et al., 2000)。

在自由基攻擊 DNA 層面，若 ROS 利用氫氧基與 DNA 上的 guanosine 之第八個碳結合則會形成穩定的 DNA 氧化傷害產物 8-oxoguanine，其水解產物 8-OHdG 會分佈於血液、組織及尿液中(Chiou et al., 2003)，由於 8-OHdG 目前被許多研究廣泛代表 DNA 氧化傷害的生物標記(Cheng et al., 1992)以及穩定的生物指標(Cooke

et al., 2000)。若 DNA 損害沒有進行修補，在細胞分裂後可能會造成突變，若突變發生在重要致癌基因或抑癌基因位置上，突變的細胞就有可能形成腫瘤，若 guanosine 受到氫氧自由基攻擊約有 0.76%的突變機率，是正常鹼基的 32 倍突變機率，且造成突變情形中 G 到 T 的 transversion 將近佔 96%(Cheng et al., 1992)，因此 8-OHdG 最主要導致 G:C 到 T:A 的 transversion 突變(Bruner et al., 2000)，且 G 到 T 突變是在抑癌基因中最常見的突變位置，因此認為 8-OHdG 與癌症發生很有相關(Loft & Poulsen, 1996)。

因為 8-OHdG 是一個廣泛被當成 ROS 對 DNA 造成氧化傷害的指標，尿液中 8-OHdG 的濃度增加與暴露有毒化學物質如多環芳香烴、吸菸等有關。8-OHdG 也可用來作為暴露環境中致突變物質之早期生物效應型標記，而測量 8-OHdG 可經由非侵入性取得檢體，但唯一缺點是因為呼吸作用粒腺體不停釋放大量 ROS，因此體內 8-OHdG 的背景值高，而造成受損的細胞或組織無法偵測到 8-OHdG 濃度顯著增多。Cheng(1992)等估計人體每天每個細胞的 DNA 受到氧化攻擊次數約 104，因此形成 DNA 核甘酸氧化產物，這些傷害絕大部分可經由 DNA 修補機轉修復，經核酸外切酶(exonuclase)切除後形成水溶性 8-OHdG 再經由尿液排出，所以分析尿中 8-OHdG 仍可反映良好的細胞氧化壓力(Rozalski et al., 2002)。

過去許多研究發現，當暴露於化學污染物質（多環芳香烴或苯）(Lagorio, 1994; Liu et al.,1996; Zhang et al., 2003)、游離輻射(Yatsuzuka et al., 2004)或抽菸(Loft et al., 1996)都會使體內 8-OHdG 濃度增加。而針對特殊職業進行的研究，例如公車司機或計程車司機，發現其體內 8-OHdG 濃度顯著高於對照組(Chuang et al., 2003)；於動物實驗也發現相同結果(Aoshiba et al., 2003)，因此檢測之 8-OHdG 不僅可評估基因毒性，也可代表環境暴露突變物質之生物有效劑量（Biological effect dose），是個很好的癌症預防標記；但其受許多因素影響，文獻中常提及之因素為吸菸、年齡、BMI、飲酒、運動、營養品補充、職業暴露及嚼檳榔等，但有些因素呈現正相關、負相關或未達顯著相關性，各不同研

究中影響 8-OHdG 之因素整理歸納如表 2。

## 第四節 游離二氧化矽之基因及免疫毒性

一般游離二氧化矽被人吸入肺部，二氧化矽表面會與肺部細胞、肺部內組織液產生反應，以形成(Si-OH)(Si-O-)等官能基，進而產生氫氧基或過氧化物(Donaldson et al.,1998)。Castranova et al.(2000) 亦利用細胞培養及動物實驗，將游離二氧化矽毒性分為細胞毒性、基因毒性、致癌性；該研究認為游離二氧化矽可直接造成肺部細胞之脂質過氧化，或刺激肺泡巨噬細胞產生 ROS，或刺激肺泡巨噬細胞或上皮細胞產生發炎因子及纖維化因子，造成組織損害、肺部纖維化及基因傷害。可呼吸游離二氧化矽會引起矽肺症，其引起細胞傷害的可能機制有：1. 游離二氧化矽直接的細胞毒性。2. 游離二氧化矽對巨噬細胞的刺激以及細胞毒性酵素或氧化物之釋放。3.巨噬細胞的刺激造成補充多型核白血球的發炎物質之釋放，這些物質可能釋放細胞毒性物。4.巨噬細胞的刺激釋放出新的組織纖維母細胞產生以及膠原的合成。

而游離二氧化矽對細胞的危害，主要在於其表面會經由一連串反應而產生自由基與氧化壓力，進而損害細胞。Schins et al.(2002)以 ESR 量測含游離二氧化矽粉塵表面之氫氧基，並藉以測定 8-OHdG、乳酸去氫酶 (LDH, lactate dehydrogenase)、以彗星分析(Comet Assay) DNA 損害情形，證實該粉塵對 A549 人類上皮細胞造成之細胞毒性及基因毒性；而當顆粒表面加以乳酸鋁處理，則可以顯著降低游離二氧化矽所造成之細胞毒性及致癌性。

Driscoll(1990)根據先前的體外及活體試驗研究之結果推論出老鼠因游離二氧化矽暴露造成肺部腫瘤的假設機制，游離二氧化矽造成肺部腫瘤是因為發炎細胞聚集與活化後繼而引起的，發炎細胞之存在導致肺部細胞生成之氧化物、細胞激素、生長因子增加，氧化性物種生成為增加肺部細胞毒性與基因毒性之機制。

如前 Fubini 及 Hubbard(2003)所提及暴露二氧化矽後，可能引起的細胞反

應，巨噬細胞可能會釋放 ROS、RNS、細胞激素…等最後會造成細胞凋零或死亡以及二氧化矽微粒之釋出，因此細胞激素可視為肺部傷害之先兆。在 Zhang 及 Shen 研究中(2000)，指出暴露於游離二氧化矽下，其所產生之氧化壓力造成 GSH 改變，為肺部發炎之指標，進而對肺部巨噬細胞產生細胞及基因毒性。而 Johnston et al.(2000)及 Schins et al.(2002)亦分別在老鼠動物實驗及 A549 肺部上皮細胞培養研究上，皆發現其暴露於游離二氧化矽時，所造成之氧化傷害使巨噬細胞（AM）、嗜中性粒細胞（PMN）產生之數量增多，且造成 DNA strand 斷裂。

游離二氧化矽微粒可能引起急性與慢性的肺部發炎反應(Adamson et al., 1984; Morgan et al., 1980)，可能會引起肺部纖維化的情形。而肺泡巨噬細胞扮演肺部發炎以及纖維化進展的一個重要的角色，二氧化矽進入肺泡內會激發肺部巨噬細胞與表皮細胞形成細胞激素，使發炎細胞的產生，增加發炎反應。研究指出肺泡巨噬細胞是發炎反應以及肺部纖維化的一個重要角色，游離二氧化矽進入肺泡時，會激發肺部巨噬細胞與表皮細胞形成細胞激素，使發炎細胞的產生增加發炎反應（TNF-$\alpha$、IL-6）（Du and Wang，2003）。由人體或動物體內取出紅血球去暴露無機灰塵(包含游離二氧化矽、石綿)微粒約 1-4 小時，細胞溶解之狀況以血紅素被釋放出的量來評估，而體外試驗是以巨噬細胞暴露到游離二氧化矽之細胞毒性分析來進行，巨噬細胞受到刺激後釋放細胞激素可以做為細胞毒性的評估。細胞激素是細胞與細胞間溝通，細胞變異和細胞生殖的重要調節因子。TNF 則是巨噬細胞釋放的激素中一種，巨噬細胞釋放之細胞激素不僅有 TNF，另外還有 IL-6 及 IL-10，所以暴露到游離二氧化矽或其他微粒都可能刺激這些細胞激素產生。從肺部纖維化的病人身上萃取出被活化的肺泡巨噬細胞，以及釋放出多種的纖維化因子與細胞激素。在這些激素中 TNF-$\alpha$ 為游離二氧化矽導致的發炎及纖維化反應很重要的調節者。游離二氧化矽的暴露可能會引起 TNF-$\alpha$ 釋放、NF-$\kappa$B 活化以及細胞凋零的機制。另外在基因轉殖的老鼠肺部發現 TNF-$\alpha$ 的過度表現導致肺泡之分裂及緩和肺部纖維化(Miyazaki et al., 1995)。

Johnston et al. (2000)針對游離二氧化矽對肺部之危害，在老鼠之肺部沖洗液中之嗜中性球(neutrophils)、多型核白血球 (polymorphonuclear leukocytes,PMNs)、乳酸脫氫酵素(lactate dehydrogenase,LDH)濃度，指出游離二氧化矽具有細胞毒性，且其危害為非游離二氧化矽之兩倍。而 Cakmak et al.(2004)在其 A549 上皮細胞研究上，藉由 LDH、MTT(metabolic substrate)的測定，結果顯示游離二氧化矽暴露造成細胞質破壞，故其具有細胞毒性。在國內，則蘇等(2002)針對鋼鐵廠修爐工人進行尿液檢測，發現其 $PGF_{2\alpha}$濃度與作業環境之可呼吸性粉塵、游離二氧化矽暴露量呈現正相關。

通常巨噬細胞的自我凋零是矽肺症發病一個早期的可能情形。如一研究指出在暴露吸入性游離二氧化矽後 10 天，在老鼠的肺部發現凋亡的巨噬細胞，在暴露 56 天後肺部組織中肉芽腫性細胞也發覺凋零的現象。相較之下，細胞自我凋零之誘發與其後被新招募的巨噬細胞移除掉凋零之細胞，這一種急性肺部發炎反應如同一個肺部發炎清除的過程，可能建議細胞凋零過程幫助了修復的步驟。細胞自我凋零反應發生在矽肺症發展的早期可能表示試圖移除受傷害之細胞和清除發炎反應，導致組織改組以及維持肺部功能(Huaux,2007，如圖 2)。

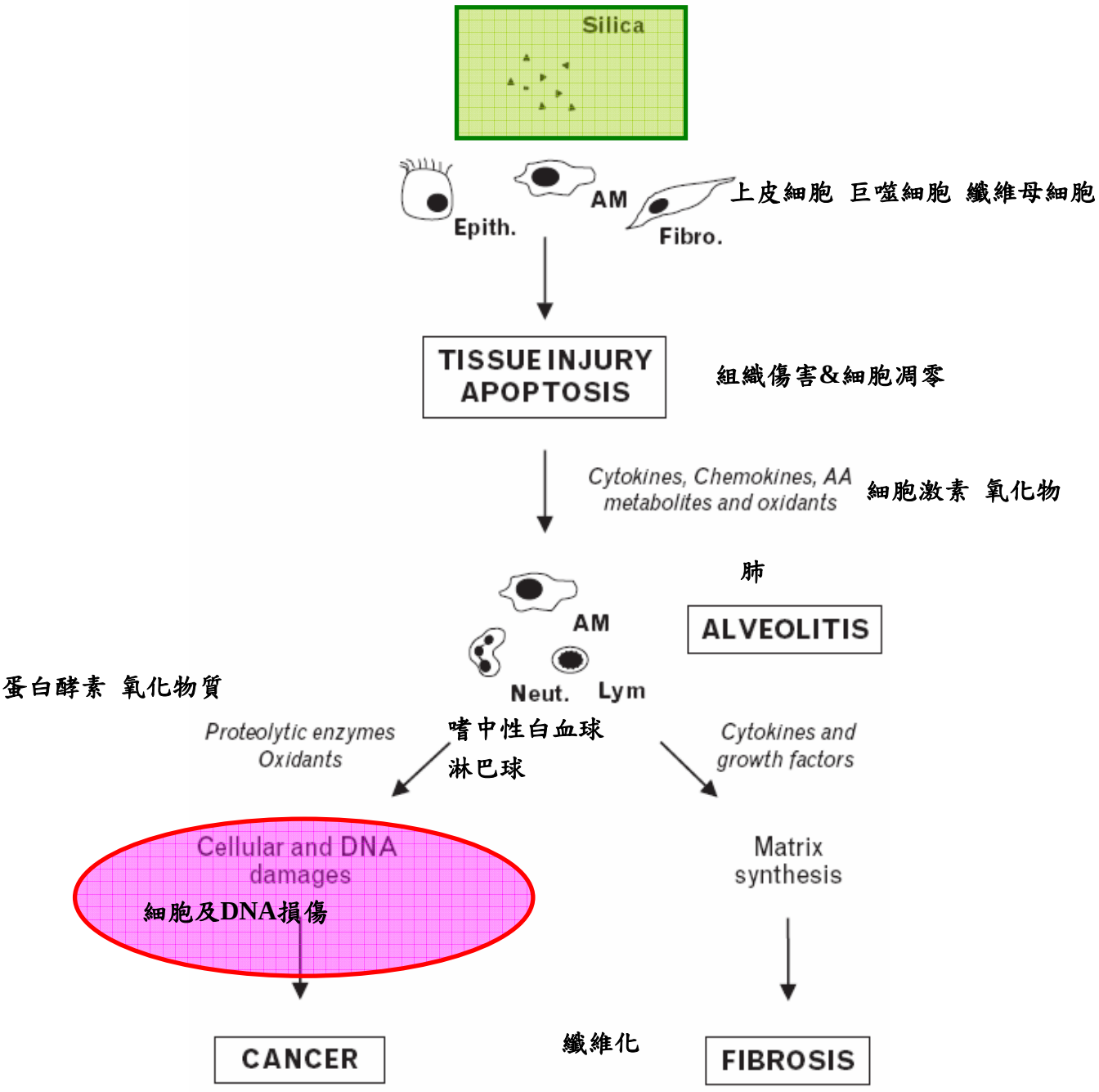



圖 2 游離二氧化矽致病機轉

游離二氧化矽在人體內是一個已知的肺部纖維化疾病原因，而在老鼠的實驗上亦已經證明吸入游離二氧化矽是有致癌性的(Johnson et al., 1987)。在 1995 年，Nagalakshmi 等人(1995)，利用中國大鼠的肺部纖維母細胞（V79）以及人類的胚胎肺部細胞（Hel299）以兩種游離二氧化矽四種濃度去做處理，兩種游離二氧化矽在 160 $\mu$g/ cm$^2$和 320 $\mu$g/cm$^2$濃度下造成老鼠與人類的細胞都有微小核的形成，並且也發現游離二氧化矽濃度在 40 和 80 $\mu$g/cm$^2$中，細胞微小核有顯著性的增高，先前其他研究也發現石英與哺乳類動物細胞一起在試管中培養，可能具有誘發細胞產生微核的能力(Hesterberg et al., 1986; Oshimura et al., 1984)。

另外， Pairon et al.等人在 1990 年針對鱗矽石與石英微粒測試其基因毒性，發現將鱗矽石與人類淋巴球與單核白血球一起培養，在鱗矽石的濃度為 5、50 $\mu$g/cm$^2$(89%的鱗矽石顆粒粒徑小於 1 $\mu$m)，會使細胞姊妹染色體交換頻率顯著增加(P＜0.05)。而體外試驗發現石英顆粒也會讓倉鼠的胚胎細胞(Oshimura et al., 1984)與小鼠的胚胎細胞(Saffiotti et al., 1995)之型態轉變，並有劑量效應相關。Xiaorong et al.等人在 1996 年發表將中國大鼠肺部纖維組織母細胞（V79 細胞）以可呼吸性游離二氧化矽去做處理，發現游離二氧化矽會引起染色體變異。Basaran 將暴露到游離二氧化矽的陶瓷工廠與鑄造廠員工，使用彗星試驗法去偵測 DNA 傷害之程度，發現職業上暴露到游離二氧化矽的員工有 DNA 損害增加的情形，並且吸菸是另外的一個危險因子(Basaran et al., 2003)，所以在本研究中亦會針對吸菸習慣納入統計處理。綜合各研究探討如表 3 所示。亦有文獻指出，工人暴露含鈷化合物後會造成體內 DNA 氧化性傷害，且研究中也將多種 DNA 傷害指標(例如：尿中 8-OHdG、彗星試驗及微小核分析)進行相關性探討，結果發現：尿中 8-OHdG 濃度與彗星試驗分析中的尾部長度(TL)與尾部動量(TM)有統計上顯著相關(De Boeck et al., 2000)。

到目前為止，已有許多技術被應用來評估物質對 DNA 的傷害，如：染色體變

異、微核試驗、姊妹染色體互換、突變測試等(Tice et al., 2000)。目前由於彗星試驗分析方法的建立，使其成為較準確且快速辨識基因毒性的方法 (Rojas et al., 1999) ，能夠快速的容易測量個體細胞 DNA 傷害之程度，所以在本次研究中採用彗星試驗來偵測職業上暴露游離二氧化矽的情形。

在 1984 年，彗星分析法首先由 Ostling 和 Johanson 所提出(Ostling & Johanson, 1984)，是一用來檢測 DNA damage 的技術。已被證明是一敏感、簡單、快速且能直接觀察單一細胞基因毒性的分析方法(Rojas et al., 1999)。首先利用 agarose 將細胞包埋在其中，接著將細胞 lyse，之後再以電泳法處理；若 DNA 上有損害，則其破碎的片段會藉由電泳時被拖出細胞，經由染色後在顯微鏡下則呈現出類似彗星的形狀，此即為稱之彗星分析法的原因。不同程度的傷害會造成 DNA 拖尾程度的差異，因此，利用其拖尾的程度便可評估細胞 DNA damage 的嚴重性(Wiklund & Agurell, 2003)，但該結果亦會受到年齡、性別、運動、飲食、抽菸…等影響(Moller et al., 2000)。

彗星試驗的干擾因子可能有以下(Peter et al., 2000)：

**年齡**

有一美國研究發現 41 位研究對象其年齡的範圍介在 24-93 歲之間，將研究對象以年齡（60 歲）作區分，發現＞60 歲的人其 DNA 損傷比＜60 歲的人的 12 倍。總體來說，研究對象的年齡似乎對 DNA 損傷的平均基本程度沒有太大影響。在 2001 年印度的研究中將 62 位健康的男性根據其年齡分成四組，依序為 20-29、30-39、40-49、50 歲以上，發現後三組的 DNA 傷害都比第一組高(Dhawan et al., 2001)。

**空氣污染**

有研究顯示空氣中 PAH 的濃度與 DNA 損害的關係，在一 542 個研究個案之研究中，顯示出空氣污染對 DNA 的損傷情形，即使控制了 GSTM1 基因多型性、抽菸以及種族背景結果仍然一樣。

**飲食習慣**

每日補充超過 350mg 的維生素 C 對 DNA 損害以及 $H_2O_2$ 或游離輻射的抵制並無影響，反之，維生素 C 500-2000mg 之單一劑量在 2-4 小時之後，$H_2O_2$ 或游離輻射的抵制有增加的情形，類胡蘿蔔素添加劑與富含類胡蘿蔔素之蔬菜產品可以減少 DNA 損傷。

**運動習慣**

過量的運動與氧化壓力有關，反應了較高程度的氧化性 DNA 傷害以及脂質過氧化；在跑步完 5 公里後，有三分之一的人約 5 分鐘其血液樣本中的 DNA 損害會有增加的情形。

**性別**

一個大型的橫斷性研究說到男人比起女人有較多的 DNA 損害情形，顯示出男性有較寬的 DNA 損害距離，與這一個義大利研究相對比的是說明女生有較多的基本 DNA 損害。最後總結似乎女性有較高的 DNA 損害程度。

**吸菸習慣**

在希臘的研究報告中對 20-25 歲和 55-60 歲兩群健康者做彗星試驗，發現吸菸者都有較高的 DNA 傷害，並在扣除掉年齡的影響後，發現吸菸的貢獻是 25.8% (Piperakis et al., 1998)。Betti et al.等人 (1995)，對一群健康者進行彗星試驗分析，結果發現，吸菸者有較多的 DNA 傷害，戒菸的人在停止吸菸一年後，其 DNA 損害程度會減低。

## 第五節 影響肺功能表現之生活因子

許多流行病學研究皆指出暴露於空氣污染物容易導致肺部疾病，特別是阻塞型肺部疾病，或是由各地區沙塵暴來臨時，醫院之看診及住院率增加可以看出大氣中這些粉塵顆粒及其上所含之化學物質、內毒素等等皆會影響人類之呼吸系統的健康(Chang et al., 2006; Yang, 2006)；特別是年長者或是氣喘過敏等患者，其健康危害之症狀會特別明顯(Costa and Kodavanti, 2003)。根據研究文獻指出，暴露於粉塵顆粒導致於肺部疾病，主要因為粉塵所含之自由基、化學物質、重金

屬等,其在呼吸系統會導致肺部之氧化傷害(Gulumian, 1999;Kelly and Sandstrom, 2004)。而人體在自由基攻擊及抗氧化酵素作用下將取得平衡，若是自由基過多攻擊而使氧化、抗氧化間失去平衡，將會使肺部導致氧化傷害、DNA 傷害(Gromadzinska and Wasowicz, 2003; Risom et al., 2005；Huffman et al., 2006)及肺部疾病。雖然自由基攻擊會導致氧化傷害，但研究指出人體可藉由攝取維他命 C、E、β-胡蘿蔔素、砷等攝取而使體內血液中之抗氧化能力提升(Romieu and Trenga, 2001; Aydin et al., 2004)，而一般日用飲食對於具抗氧化能力之維他命攝取量，也影響了肺功能表現。文獻指出，維他命攝取較量較低之孩童，他們的 FVC 相對較低(Gilliland et al., 2003)；而在肺部功能與阻塞研究上，亦指出抗氧化物質之攝取量越多，則 FEV1 之衰減風險越低(Guenegou et al., 2006)。主要在於抗氧化物質之攝取，提供了肺部氧化傷害的保護。根據中國 69 個農村橫段式之研究發現維他命 C 攝取量與肺功能表現具相關性，維他命 C 之攝取能有效防止肺功能之衰減(Hu et al., 1998)；但在吸菸者身上則無此相關性存在。而在立陶宛研究中亦可佐證抗氧化與氧化傷害成反比，其血液中之胡蘿蔔素濃度與其尿中 8-OHdG 呈現反比之趨勢(Kristenson et al., 2003)。

而 Lerman(2003)觀察鑄造廠勞工，其暴露較多粉塵顆粒者，相對較易罹患阻塞型肺部疾病。因此 Rosenman 有關鑄造廠勞工之流行病學研究，提出於鑄造廠工作 40 年後罹患矽肺症之風險為工作 20 年之風險的 1.45 倍[51]。根據 Kuo(1999)及林(1996)等人研究指出，鑄造廠勞工因為職場暴露於粉塵作業場所，導致其勞工肺功能下降。Kuo 等提出熔爐及造模製程之工人，其 FVC 和 FEV1 顯著減少。而台灣中部鑄造廠有 8.8%之勞工，因職場粉塵暴露而導致肺功能損傷甚至塵肺症。

而於陶瓷工人之研究中亦指出職場勞工若能每日飲食適時攝取抗氧化之蔬菜水果，對於提升他們的肺功能有所幫助。除了每日飲食習慣及職場暴露情況會影響人體肺功能外，本身之肥胖(Jones and Nzekwu, 2006; Lin et al., 2006; Thyagarajan et al., 2008; Pistelli et al., 2008; Perez-Padilla et al., 2006)及年齡等也多會影響肺功能表現。根據 Pistelli(2008)等人對於肥胖與肺功能關係之八年追蹤過程中，發現肥胖者減輕體重後，其肺功能將明顯改善。而在年輕族群中，肺功能受 BMI 增加也呈現負面影響(Perez-Padilla et al., 2006)。因

為太多因子會影響肺功能表現，諸如營養狀況、生活型態、BMI 以及外在環境等等(Lesgards et al., 2002)；因為肺功能變差是阻塞型肺部障礙之徵狀之一，因此在本研究中，除了考慮職場粉塵、游離二氧化矽暴露外，也一併收集勞工之日用飲食蔬果攝取情形、維他命等抗氧化補充、BMI、抽菸習慣等，同時也量測勞工肺功能、氧化傷害指標及抗氧化能力以探討彼此間之相關性。

# 第三章 材料與方法

## 第一節 研究設計與對象

1 本研究採自願參加方式招募研究對象，收集 3 家(A、B、C)鑄造廠廠共 74 名勞工為研究對象，進行胸部 X 光、肺功能、血液常規、生化、氧化傷害等橫斷式研究，了解肺功能與飲食攝取、氧化傷害、抗氧化能力指標、職場暴露、身體質量指數等相關性。而亦針對 B 廠其中 27 名勞工進行 DNA 損傷、細胞激素分析，以了解 DNA 損傷、免疫毒性與職場暴露之相關性。同時針對 A 廠進行縱斷式研究，在作業環境改善前及後進行肺功能及尿中 8-OHdG 等檢查；追蹤該廠作業員工之肺功能及 8-OHdG 濃度在工程介入後其健康之影響變化。

2 血液及尿液收集與保存:基於配合工廠之意願及作業需求無法於週五前往採樣，若能於週五進行生物檢體採樣較佳，因較能反應一週來工作暴露之影響，並可降低週末生活型態之影響。要求研究對象抽血前一晚起禁食 10 小時，一早於工廠上工前先測量研究對象之身高、體重、肺功能；繼收集體檢時一泡尿液 50ml 及 4 管血液 30ml。本研究檢體採集完成後，在運送過程中均保持 4℃，並在八小時內送回實驗室的-80℃冰箱中；在實驗的過程中，將尿液及血液分裝在數管 5c.c.之小管，減少冷凍及解凍的次數且分別放在不同-80℃冰箱內，以保持檢體的穩定性。血液方面，採集完立即送實驗室，其中有關肝功能等血液生化檢查部分係送聯合檢驗中心施測；其餘血樣經每分鐘 3000 轉的速度離心 20 分鐘後，將血清分離分裝於塑膠小瓶中。血液檢體分裝後，置於-80℃冷凍櫃中凍存，直至實驗分析時再取出。

## 第二節 實驗流程與原理

I. **問卷：**問卷資料分成個人基本資料、工作史、疾病史、自覺症狀及日用飲食

攝取頻率等部份。詳如附件一。

## II. 可呼吸性粉塵游離二氧化矽分析

以 Nylone 旋風式可呼吸性粉塵採樣器連接 37-mm 濾紙採樣匣 (37-mm filter cassette, SKC Inc.) 以封膜 (Sealing band)封住採樣匣再進行採樣，其所使用採樣介質皆為孔徑 0.5μm 聚氯乙烯 PVC 濾紙(Part No. 225-8-01, SKC Inc.) 採樣流率 1.7 L/min。採樣時段為早上 8:00 左右到下午 4:00 左右，為時約 6 小時(在此為配合工廠作息，僅能以此 6 小時反應勞工之八小時時量平均暴露濃度)。採樣器之佩帶方式為將 PUMP 繫於員工後方腰帶上 (以方便員工作業)，再將連接管繞道前方胸前，將採樣器別於員工呼吸帶處(如衣領上)，將採樣口朝前方，並避免員工遮蓋住採樣口。

可呼吸性粉塵游離二氧化矽分析依據 NIOSH 7500 與 OSAH ID-142 方法，以 X-ray 繞射儀(XRD)進行樣本分析。

### 一、實驗器材 (含設備，儀器與試劑)

(1)X-ray 繞射儀 (Rigaku corporation, GN4013A1, V1,Tokyo, Japan)

(2)電腦設備 (JCPDS-International Center for Diffraction Data Power Diffraction File, JCPDS, Swarthmore, PA. USA)

(3)高溫灰化爐

(4)烘箱 (CHIH CHIN H&W Enterprise Co. LTD., Taipei, ROC)

(5)超音波震盪器 (BRANSON 8200, Branson Ultra Sonics Corporation, Danbury, CJ. USA)

(6)磁力攪拌器與磁性攪拌石 (Model HP-11515B, Sybron/Thermolyne, Dubuque, IA. USA)

(7)抽氣過濾設備 25mm (Millipore Corp., Bedford, MA. USA)：

－ Filter Holder Hydrosol Manifold (Cat. No. XX25 04700)

－ Filter Clamps (Cat. No. XX10 025 03)

－ Fritted glass base 與 stoppers (Cat. No. XX10 025 02)

－ Glass funnels (Cat. No. XX 10 025 11)

(8)分析微量天平 (METTLER TOLEDO AT20, Mettler Toledo Co., Switzerland)

(9)標準品：

＊可呼吸性石英 5 μm (NIST SRM 1878a; Standard Reference Materials Program,

National Institute of Standard and Technology, Gaithersburg, MD. USA)。

＊可呼吸性方矽石 5μm (NIST SRM 1879a, Standard Reference Materials Program, National Institute of Standard and Technology, Gaithersburg, MD. USA)。

＊鱗矽石 (NIOSH, DPSE, ARDB, Cincinnati, OH. USA)

(10) 孔徑 0.45μm 銀膜濾紙(Silver Membrane) 25mm (Cat. No. 225-1802, SKC Inc., Eighty Four, PA USA)

(11)試藥級異丙醇 (Isopropano，分子式為 $C_3H_8O$，Merck KGaA, Darmstadt, Germany)

**二、標準品配製**

標準樣本的配製主要是將定量之標準品配製成異丙醇之懸浮液，將均勻之懸浮液依不同體積過濾於銀膜濾紙上，使銀膜濾紙上附有不同重量之標準品，並以 XRD 分析繞射峰強度。

**三、樣本處理**

樣本的處理主要是將樣本高溫灰化，將灰分配製成異丙醇懸浮液並過濾於銀膜濾紙後以 XRD 分析。

**設定條件**

| 設定項目 | 設定值 |
|---|---|
| 開始繞射 2θ角度 (start 2 theta) | 5.000° |
| 結束繞射 2θ角度 (stop 2 theta) | 80.000° |
| 繞設間距 (step size) | 0.01 |
| 繞射速度 (scan speed) | 1.000 |

**積分參數**

| 設定項目 | 設定值 |
|---|---|
| 閾值 (threshold values) | 5.0, 10.0 |
| 典型半高寬 (typical full width-half maximum) | 0.20 |
| 最小半高寬 (minimum full width-half maximum) | 0.08 |
| 繞射峰間距 (peak span) | 15 |

**四、定性與定量**

***石英、方矽石、鱗矽石定性所需具備條件***

| 名稱 | 項目 | 主要繞射峰 | 次要繞射峰 | 第三繞射峰 |
|---|---|---|---|---|
| 石英 | 2 θ | 26.66 | 20.85 | 50.16 |

| | | | | |
|---|---|---|---|---|
| (低溫) | D-spacing | 3.34 | 4.26 | 1.86 |
| | 繞射峰強度比例 | 100 | 35 | 17 |
| 方矽石 (低溫) | 2 θ | 21.93 | 36.11 | 31.46 |
| | D-spacing | 4.05 | 2.49 | 2.84 |
| | 繞射峰強度比例 | 100 | 20 | 14 |
| 鱗矽石 (低溫) | 2 θ | 21.62 | 20.50 | 23.28 |
| | D-spacing | 4.11 | 4.33 | 3.83 |
| | 繞射峰強度比例 | 100 | 90 | 50 |

**石英、方矽石、鱗矽石定量繞射峰各分別為**

| 名稱 / 項目 | 石英(低溫) | 方矽石(低溫) | 鱗矽石(低溫) |
|---|---|---|---|
| 2 θ | 26.66 | 36.11 | 23.28 |
| D-spacing | 3.34 | 2.49 | 3.83 |

**III. 肺功能測量：**肺功能以 Microspiro HI-295 (Japan)手提式肺功能機測得，FVC、FEV1 及 FEV1/FVC%等項目。在進行測量之前，儀器皆以 3 公升之唧筒進行校正，與採集尿液同一時間點進行肺功能之測試。本研究之常模採用亞洲男性，FVC(ml)=(27.63-0.112*age)*height(cm)，FEV1(ml)=34.4*height(cm)-33*age-1000。

**IV. 胸部 X 光檢查：**所有員工均接受 35X35mm 胸部 X 光檢查，檢查之胸部 X 光片由索任醫師依據國際勞工組織（ILO）於 1980 年修定之塵肺症 X 光片分類（classification of pneumoconiosis）判讀，在本研究中若 X 光片經判讀為 1/0 以上為歸類為確定塵肺症個案，0/1 則為疑似之病例。

**V. 細胞激素分析**

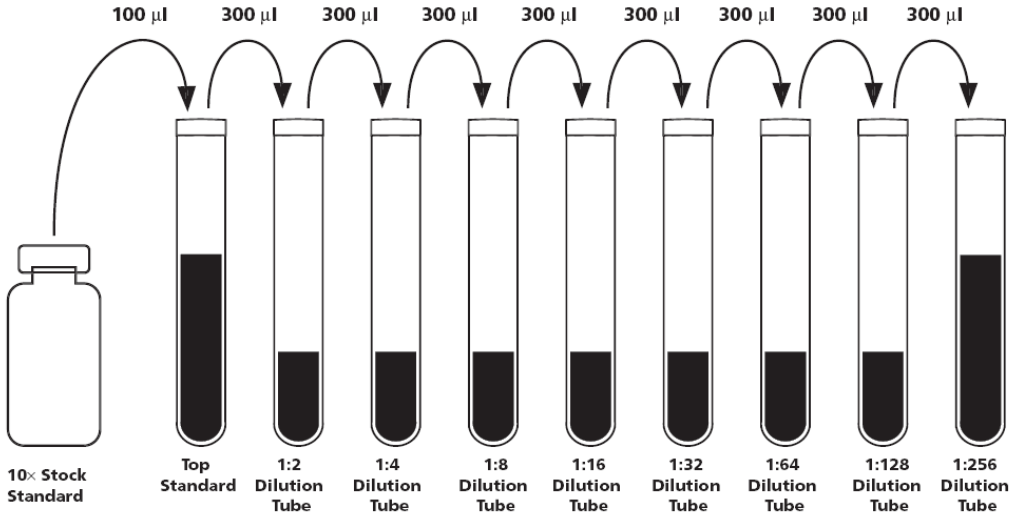
一、原理

為一種微珠多用途檢測的分析技術，利用相同大小(7.5μm)的微球上帶有不同亮度的紅色螢光強度(FL3)，分別可標識多種抗體，作為 capture beads，將血清、血漿或是細胞培養液中的抗原抓下並結合於微球表面。再以橘紅色螢光染劑(PE，FL2)或是綠色螢光染劑(FITC，FL1)標示抗體，作為 detector reagents，來偵測與微球結合的抗原並顯色。（資料來源：BD Biosciences）

二、分析步驟

(1) 標準品的配置

將 Human Th1/Th2 Cytokine Standards 以 Assay diluent 加入 200μl 去調配，靜置約 15 分鐘，不要震盪，使用序列稀釋。




將 12x75mm 之管子作標籤，分別為 Top standard,1:2,1:4,1:8, 1:16,1:32,1:64,1:128,1:256。

之後將 900μl Assay diluent 加入到 Top standard 中，剩下的管子加入 300μl Assay diluent。

再來將 10x bulk standard 取出 100μl，放入 Top standard 中，並且混合。混和完成後從 Top standard 取出 300μl 到 1:2 的管子中混合，以 1:2,1:4,1:8, 1:16,1:32,1:64,1:128,1:256 的倍數稀釋。而 Assay diluent 當作對照組。

(2) Human Th1/Th2 cytokine capture beads 混合

首先計算分析的管子（例如：未知濃度樣本有 2 管、9 管細胞激素標準稀釋液外加一管控制組，總共需要 12 管）。

在 mixed 之前，先 vortex 每一個 capture beads suspension 幾秒鐘。

將含白介素－2(IL-2)、白介素－4(IL-4)、白介素－6(IL-6)、白介素－10(IL-10)、腫瘤壞死因子(TNF)、干擾素(IFN-γ)等六種 cytokines capture beads 各取出 110μl，總共需要 660μl，再進行混合的動作。

(3) 計算 cytokines capture beads 的量為：

12 管×50μl mixed beads=600μl，為了避免取量不夠，將每一種 cytokines capture beads 多加 10μl，所以總共 660μl。

之後取出 50μl mixed Capture Beads 進入每一個分析試管的底部，再加入分析試管前需先 vortex。

加入 50μl Human Th1/Th2-II PE Reagent 進入分析試管中；以及加入 50μl Human Th1/Th2 Cytokine Standard dilution 進入控制組分析試管。

之後每個 test sample 取 50μl 進入待分析的試管中。

加完之後將分析試管靜置在室溫下 3 小時，預防直接暴露到光線。

等到作用 3 小時後加入 1ml wash buffer 進入每一個分析試管中，以及 200g 離心 5 min。

離心結束小心地將上清液倒掉（倒一次就好），加入 300μl wash buffer 進入每個分析試管使 bead pellet 再次懸浮，即可進行分析。

(4) Cytometer setup beads 之準備（校正流式細胞儀）

首先加入 50μl cytometer setup beads 進入三個試管中，分別標上 A、B、C。

之後分別加入 50μl FITC positive control detector 以及 PE positive control detector 進入 B、C 管中。

再將 A、B、C 試管放置室溫下培養 30 分鐘，以及避免直接照到陽光。最後在 A 管中加入 450μl 的 wash buffer，以及分別加入 400μl wash buffer 進入 B、C 管中。

(5) 進行樣本分析

使用流式細胞儀（BD FACSCalibur™ instrument）與該廠所附 CellQuest™及 FCAP Array 軟體進行濃度測定和細胞激素濃度轉換。

三、實驗品質管制

(1)檢量線

每一次檢量線達 $R^2$ 皆達 0.99 以上才納入分析資料中。

(2)信度檢定

血漿中細胞激素濃度分析每次實驗取 5%的樣本作重複分析一次，經過 Wilicoxon Signed Rank test 檢定達內部一致 p=0.39(n=10)。之後取樣本 10%在不同次實驗重複一次之一致性 p=0.28(n=10)。另外共七次實驗每次進行實驗之標準品分析的 CV＝10.65%。

## VI. 尿中 8-OHdG 濃度

一、原理

尿液中 8-OHdG 濃度分析實驗參考 Yin et al.(1995)發表之酵素結合免疫吸附分析法(enzyme linked immunosorbent assay; ELISA)偵測。使用 ELISA kit(Japan Institute for the Control of Aging, Fukuroi, Shizuoka, Japan ) 試劑組測定，其原理是利用競爭型抑制法 ELISA 來偵測 8-OHdG，可偵測濃度為 0.125~10ng/ml。

二、分析步驟

實驗步驟如下：首先以 50μl 尿液和 50 μl 一次抗體(8-OHdG 特定單株抗體)在 37°C 下培養 1 小時，接下來加入 250μL pH 7.4 磷酸鹽緩衝溶液(phosphate buffered saline; PBS)清洗 3 次去除結合物，接著加入 100 μl 二次抗體(以山葵根過氧化(horseradish peroxidase)標幟之抗體)，並在 37°C 下培養 1 小時，然後再以 250 μl PBS 清洗 3 次去除未結合物，並加入 100μl 呈色 (3,3,5,5-tetramethylbenzidine)，
避光(室溫下 15 分鐘)，產生淡藍色，再加入 100 μl 中止劑(1 M 磷酸 (phosphoric acid))使顏色變為黃色，反應 3 分鐘之後，測 450 nm 吸光值，30 分鐘內判讀完畢。

呈色吸光值與 8-OHdG 濃度成反比，取 8-OHdG 標準溶液 0.5、2、8、20、80 和 200 ng/ml 濃度之 log 值與吸光值作圖，再以樣本之吸光值換算出濃度，結果以 μg/g creatinine 表示。如果研究對象尿液樣本 creatinine 濃度小於 30 mg/dl 表示此為尿量極度稀釋後的樣本而不列入資料分析。

三、實驗品質管制

(1) 檢量線

$R^2$ 每次至少達到 0.995 以上，此次實驗數據才納入分析資料，若無則重新分析檢體。

(2)信度測試

尿中 8-OHdG 實驗每次取 10%樣本重覆作二次以觀察內部一致性，經 Wilcoxon 檢定(n=21)顯示 p=0.498 且 CV=8.8%，達到內部信度一致性；將 10%樣本觀察每次實驗之外部一致性，經 Wilcoxon 檢定(n=4)顯示 p=0.715 且 CV=18.7%，達到外部信度一致性。

## VII. 抗氧化能力測定

本部分由國防醫學院公共衛生研究所協助進行，血漿中總抗氧化能力為脂溶性抗氧化能力和水溶性抗氧化能力之總和，而脂溶性抗氧化能力和水溶性抗氧化能力之檢測係採商業化標準試劑組並以化學冷光(PHOTOCHEM)分析(Popov et al., 1994; Popov and Lewin, 1999)。而配置妥之試劑於實驗中維持於 4℃的環境下，並避光。脂溶性抗氧化能力之試驗步驟為：首先使用含有 EDTA 的抽血管抽取血液保存在-75℃。待分析之樣本解凍後，隨之以 200μl 的去離子水＋200μl 的 plasma ＋400μl 的 ethanol（乙醇）；之後再加入 800μl 的 hexane 己烷，震盪 1 分鐘及離心 5 分鐘（1000*g）。取上清液 550μl 使用 nitrogen 氮氣緩慢 purge 至乾燥清除有機層，再以 500μl 甲醇 methanol 溶解殘留物。震盪後隨即以 4℃保存並隨即分析。而 ACW Kit 試劑以 Ascorbic Acid 為標準，分子量 176.13 g/mol；ACL Kit 試劑以 TROLOX® 為標準，分子量 250.3 g/mol。而樣本分析之變異係數在 8% 以內。

## VIII. 彗星實驗分析 DNA 損傷情形

一、原理

彗星分析是一用來檢測 DNA damage 的技術，首先利用 agarose 將細胞包埋在其中，接著將細胞 lyse，之後再以電泳法處理；若 DNA 上有損害，則其破碎的片段會藉由電泳時被拖出細胞，經由染色後在顯微鏡下則呈現出類似彗星的形狀，不同程度的傷害會造成 DNA 拖尾程度的差異，因此，利用其拖尾的程度便可評估細胞 DNA damage 的嚴重性。

二、白血球的收集

血液，經過 1450 rpm、20℃，離心 25 分鐘之後，取出中間層(白血球)並加入 10ml RPMI Medium1640(1X)，再以 1450 rpm、20℃，離心 30-40 分鐘，離心後試管內的離心液會分為三層，取出第二層淋巴細胞層(濁白層)，再以淋巴球細胞三

倍體積之 PBS 以微量滴管上下來回沖洗，以 700 rpm、20℃，低速離心 10 分鐘，移除上清液，重複清洗淋巴球一次，最後移除上層液，留下沉澱的淋巴球細胞，加入適量的 PBS(phosphate buffer saline)以進行彗星分析法。於 24 小時內以 Ficoll solution 進行前處理，並且用 DMSO 將白血球適當的保存於-80℃的冰箱中，並於一個月內以彗星分析法來評估白血球中 DNA 損傷的情形。

三、分析步驟

先熔解 LMAgarose（置於沸水 5 分鐘），再置於 37℃水浴中使其回溫（20 分鐘）；取 1×105/ml 的細胞 50λ溶於 500λ的 LMAgarose 中，取 75λ的混和液加入 Comet Slide 樣品槽中，再將玻片平放在 4℃的暗箱中（10 分鐘），接著把玻片浸置於預冷的 Lysis buffer 中(4℃,30~60 分鐘),之後將玻片浸於 Alkaline pH 12~13 溶液中（室溫、避光，20~60 分鐘），再拿出玻片甩開沖洗掉多餘的 Alkaline pH ＞13 溶液，接著將玻片浸於 1X TBE buffer 中（一次 5 分鐘，共 2 次），最後把玻片放於水平電泳槽中 50V（10 分鐘）並將玻片浸洗於 70%的酒精（5 分鐘），然後風乾玻片，加入 50λ的 SYBR Green 溶液染色，再於螢光顯微鏡下觀察。

四、影像分析與計算

隨機選取 50 個彗星影像，利用 Komet5.5 (Kinetic Imaging Ltd, Liverpool, UK) 軟體來計算，於螢光顯微鏡下觀察，條件為 ISO100、曝光時間 1.3 秒、於 400X 下照相，並計算尾部長度( tail length)、頭尾比例(L/H)、尾部動量(tail moment)和 Oliver 尾矩(OTM)等參數。

其中：

1. 尾部 DNA 長度(tail length, TL)=彗星影像全長－頭部區域長度
2. 頭尾比例(L/H)=尾巴長度/頭部直徑
3. 尾部動量(tail moment, TM)=(尾部長度－頭部長度)×尾部亮度百分比
4. Oliver 尾矩(OTM)=(Tail mean-Head mean)*Tail%DNA100

五、實驗品質管制

(1)盲樣試驗

欲判別玻片進行重新編碼，在不知分組的情況下進行分析檢體與計數。

(2)信度測試

實驗完成後，從所有的樣本中隨機抽取 10%的玻片重複分析判讀，經 Wilcoxon 檢定(n=10)顯示 L/H p=0.799、TM p=0.159、TL p=0.59，達到內部一致性；另外，在計數完畢讓另一名經訓練後之計數員重複計數，比較兩者的一致性，經 Wilcoxon 檢定(n=9)顯示 L/H p=0.314、TM p=0.594、TL p=0.859，有達到外部一致性。

## 第三節 資料處理與統計方法

因一般生物檢體呈現右偏情形，所以由常態分布分析統計及繪出常態機率圖決定合適的統計方法（母數、無母數）。8-OHdG、彗星分析、細胞激素經常態分佈分析（Kolmogorov-Smirnov）檢定以決定是否需經對數轉換；若轉換後仍呈現不常態分佈，則選用無母數分析方法。以 SPSS for Windows 12.0 與 STAT8.0 資料統計軟體進行描述性及推論性統計分析，本研究達統計顯著差異之 P 值定義為＜0.05。另本研究案之累積暴露濃度計算為作業環境個人採樣之可呼吸性游離二氧化矽暴露濃度乘上問卷調查中進入該廠之工作年資。

1. 以次數分配（Frequency distribution）呈現暴露組與工廠別等受試者基本資料。

2. 以卡方檢定($\chi^2$ test)來比較暴露組與工廠別的人口學變項（類別變項）之差異。

3. 以 t 檢定（t test）來比較暴露組、工廠別的人口學變項及（連續變項）肺功能、8-OHdG、comet assay、cytokine 數值等結果是否有差異。

4. 以複迴歸(multivariate regression analysis)來分析，在控制

年齡、性別、吸菸情形...等因素後，觀察暴露組別、工廠廠別、改善前後及累積暴露濃度等之肺功能、8-OHdG、comet assay 與 cytokine 等是否有差異。

5. 以相關係數(Pearson correlations)分析，觀察研究對象的 8-OHdG、彗星分析數值(L/H、TM、TL) 與 cytokine 有無相關。

6. 以 Generalized Estimation Equations (GEE)模式來調整年齡、性別、吸菸情形，觀察研究對象在工程改善前後重複測量勞工的肺功能、8-OHdG 濃度是否有差異。

# 第四章 結果與討論

## 第一節 研究對象之基本資料及肺功能健康

本研究案共收集三個鑄造廠之勞工問卷及生物檢體，如表 4 顯示，該鑄造業族群平均年齡為 47.64±10.0 歲，平均工作年資為 19.15±11.1 年，身體質量指數(BMI)平均為 24.94±2.9kg/$m^2$，累積暴露濃度平均為 12.33 ±8.9 mg/$m^3$*year(本研究案之累積暴露濃度為作業環境個人採樣之可呼吸性游離二氧化矽暴露濃度乘上問卷調查中進入該廠之工作年資)。而具有吸菸習慣之勞工為 29 人(39.2%)，有吃檳榔習慣之勞工為 19 人(25.6%)，有攝取維他命 C、維他命 E、綜合維他命之勞工分別為 10 人(13.5%)、5 人(6.7%)、14 人(18.9%)。至於教育程度，本族群勞工(含)國中以上者佔 33 人(44.6%)。

若將 74 名勞工區分為吸菸者及非吸菸者，兩組在年齡、工作年資、BMI、累積暴露濃度、教育程度、各種維他命攝取等並無顯著差異；僅在嚼食檳榔習慣上，吸菸勞工比非吸菸勞工明顯有較高的百分比(p 值=0.0007，如表 4)。而以廠別區分，A 廠 19 人、B 廠 28 人、C 廠 27 人，共計有 74 人（如表 5）。其中包括作業類別為：拆模、噴砂、研磨之暴露 10 人（13.5%），造模、合模、噴模、電爐、燒鑄之暴露 40 人（50.1%），其他的行政清潔人員 24 人（32.4%）。

### 一、不同廠別之描述及檢定

將研究對象之基本人口學變項及肺功能、氧化傷害、抗氧化能力依據不同廠別描述及檢定如表 5。以 A 廠勞工為例，其中勞工平均年齡為 41.41±13.34 歲、平均工作年資為 11.42±7.75 年、平均 BMI 為 24.69±2.89kg/$m^2$、FEV1 平均為 3.34±0.74L、FVC 平均為 3.95±0.83L、FEV1%平均為 96.5±13.3%、FVC%平均為 100.82±16%、FEV1/FVC%平均為 84.7±5.7%、8-OHdG 平均為 15.6±15.7ng/ml、8-OHdG/Cr 平均為 6.46±5.82μg/g、TAC 平均為 62.21±26.1。

經過檢定可發現在年齡(p 值＝0.01)、工作年資(p 值＜0.0001)、累積暴露類

別(p 值＜0.0001)、教育程度(p 值=0.047)、婚姻狀況(p 值＝0.006)、罹患塵肺症比例(p 值=0.04)、FEV1(p 值=0.0006)、FEV1%pred(p 值＜0.0001)、FEV1/FVC%(p 值＜0.0001)這些選項上，A、B、C 三廠間有明顯差異。在年齡、工作年資方面，B 廠明顯高於另兩廠；在累積暴露類別方面，B 廠高暴露組百分比亦相對明顯高於另兩廠；在教育程度方面，C 廠較高比例在國中以下；在婚姻狀況方面，A 廠相對 B、C 兩廠有較高比例屬單身者。至於在罹患塵肺症比例方面，B 廠罹患比例明顯高於另兩廠。在肺功能之 FEV1、FEV1%pred、FEV1/FVC%方面，B 廠勞工之肺功能表現明顯低於另兩廠；但在 FVC、FVC%pred 方面，三廠勞工之肺功能表現並未明顯差異。而在氧化傷害與抗氧化能力方面，三廠勞工間也是未有明顯差異。

而在肺功能各變項、氧化傷害及抗氧化能力方面，將三廠之勞工再區分為吸菸者及非吸菸者；承續如表 5，可以了解到不論 A、B、C 工廠，其同一工廠中勞工肺功能及氧化傷害健康表現之分佈並不因吸菸、不吸菸與否及該廠所有勞工等彼此間有何顯著差異。但在 FEV1、FEV1%pred、FEV1/FVC%三變項方面，可以看出凡是吸菸族群、不吸菸族群及該廠所有勞工，皆在 A、B、C 三間不同工廠間存有顯著差異之情況。如 FEV1 變項為例，吸菸族群、不吸菸族群及該廠所有勞工，皆在 A、B、C 三間不同工廠間檢定之 p 值分別是 0.03、0.03、0.0006，在不同工廠間呈現顯著差異。而在氧化傷害(8-OHdG、8-OHdG/Cr)及抗氧化能力方面，吸菸族群、不吸菸族群及該廠所有勞工等在 A、B、C 三間不同工廠間未有顯著之差異。

將肺活量 FVC%＜80%視為異常，而該變項之正異常百分比分布依工廠廠別之檢定，三工廠間並無顯著差異(表 6)；其中 A 廠有 2 名異常、C 廠有 1 名異常者。另將 FEV1/FVC%＜70%視為異常，而該變項之正異常百分比分布依工廠廠別之檢定，三工廠間存在顯著差異；其中 B 廠有 14 名(50%)屬於異常，其餘 A、C 廠並無異常者。而將 FEV1/FVC%＜70%且 FVC%≧80%歸類為阻塞型肺功能障礙，FEV1/FVC%≧70%且 FVC%＜80%歸類為限制型肺功能障礙，FEV1/FVC%＜70%且 FVC%＜80%歸類為混合型肺功能障礙，FEV1/FVC%≧70%且 FVC%≧80%歸類為肺功能正常。在三工廠

間之分布(表 7)，A、C 廠各有 2、1 名限制型肺功能障礙者，而 B 廠有 14 名阻塞型肺功能障礙者；各廠間在此分類之分佈表現具顯著差異。總 74 名勞工中，有 14 名(18.9%)阻塞型肺功能障礙者、3 名(4.1%)限制型肺功能障礙者，其餘 57 名(77%)肺功能正常。

在本研究中，欲了解游離二氧化矽及粉塵對於勞工造成之氧化傷害及 DNA 傷害，在此以尿中 8-OHdG/Cr 濃度來代表其傷害之程度。而影響尿中 8-OHdG/Cr 濃度因子依不同廠別之描述與檢定，結果如表 8　顯示，A 廠勞工之 8-OHdG/Cr 平均濃度為 6.46±5.82g/g creatinine、B 廠勞工為 4.1±1.89g/g、C 廠勞工為 5.14±3.45g/g。將影響尿中 8-OHdG/Cr 濃度之可能因子如年齡、BMI 等納入分層，觀察其於各分層勞工之 8-OHdG/Cr 濃度值分佈；至於吸菸習慣、吃檳榔習慣之有無及肝功能、肺功能正異常之呈現亦一併納入分層觀察其 8-OHdG/Cr 濃度值分佈。除了年齡＞55 歲之勞工在 A、B、C 不同三廠間之濃度值分別為 1.22±0.45g/g、4.87±1.39g/g、8.44±1.74g/g，具顯著差異(p 值=0.006)。其餘不管是各影響因子變項之習慣有無或正異常與否，其在同一工廠分層之濃度值並無顯著差異，而即使在各不同工廠間也是無顯著差異存在。

**二、不同累積暴露組別之描述及檢定**

我們將所有 74 名勞工游離二氧化矽累積暴露量之分佈分組，在 0～25%之間為低暴露組、25～75%之間為中暴露組、75～100%之間為高暴露組；低暴露組之累積暴露濃度≦5.38 $mg/m^3$*year，中暴露組之累積暴露濃度介於 5.38~18.54 $mg/m^3$*year 之間，高暴露組之累積暴露濃度≧18.54 $mg/m^3$*year。低暴露組包括 19 名、中暴露組包括 35 名、高暴露組共 20 名。

我們將研究對象之基本人口學變項及肺功能、氧化傷害、抗氧化能力依據不同累積暴露組別描述及檢定，結果如表 9。以高暴露組 20 名勞工為例，其中勞工平均年齡為 53.3±9.31 歲、平均工作年資為 29±6.76 年、平均 BMI 為 24.22±2.18$kg/m^2$、FEV1 平均為 2.68±0.61L、FVC 平均為 3.84±0.79L、FEV1%平均

為 91.1±12.1%、FVC%平均為 107±16.4%、FEV1/FVC%平均為 70.5±10.3%、8-OHdG 平均為 10.3±8.7ng/ml、8-OHdG/Cr 平均為 5.12±3.32μg/g、TAC 平均為 55.6±21.6 m mole Trolox/g。

經過檢定，可以清楚看到鑄造業總勞工在年齡、籍貫、工作年資、教育程度、HBsAg、FEV1、FEV1%pred、FEV1/FVC%這些選項上，高、中、低三暴露組間有明顯差異。由於本研究之累積暴露濃度係以勞工個人游離二氧化矽暴露濃度乘上其在該廠之工作年資，所以會導致高、中、低三暴露組在年齡、工作年資方面皆有顯著差異的影響。而在教育程度方面，高暴露組擁有國中以上程度之比例相對較高。在肺功能之 FEV1、FEV1%pred、FEV1/FVC%方面，高暴露組勞工之肺功能表現明顯低於另兩中、低暴露組；且趨勢檢定亦呈現低中高暴露組之肺功能表現越來越差之趨勢(如表 17)，趨勢檢定之 p 值分別為 0.002、0.003、＜0.0001。但在 FVC、FVC%pred 方面，三暴露組別勞工之肺功能表現並未明顯差異。而在氧化傷害與抗氧化能力方面，三暴露組勞工間也未有明顯差異。

而在肺功能各變項、氧化傷害及抗氧化能力方面，將三暴露組別之勞工再區分為吸菸者及非吸菸者；承續如表 9，可以了解到不論高、中、低三暴露組，其同一暴露組族群中勞工健康表現之分佈並不因吸菸、不吸菸與否及所有勞工等彼此間有何顯著差異。而其中 FEV1/FVC%該變項在高暴露組中，吸菸、不吸菸及所有勞工族群分別為 60.7±10.7、73.8±8.12、70.5±10.3%，經檢定，其 p 值=0.06 介於邊緣值附近。FEV1、FEV1%pred、FEV1/FVC%三變項在 74 名勞工之高中低暴露分組間雖有顯著差異，但若將樣本數再細分吸菸與否，則 FEV1、FEV1%pred 在非吸菸勞工方面未達顯著差異，其 p 值分別為 0.09、0.09，皆介於邊緣值附近。而在 FEV1/FVC%變項方面，可以看出凡是區分為吸菸勞工、不吸菸勞工及所有勞工，皆在高、中、低三暴露組間存有顯著差異之情況；如以吸菸族群而言，其在高、中、低暴露組分別為 60.7±10.7、80.7±9.7、84.9±5.2%，其 p 值=0.004。吸菸勞工、不吸菸勞工及所有勞工，在高、中、低三暴露組間檢定之 p 值分別是 0.004、0.0004、

＜0.0001，在各不同暴露組間皆呈現顯著差異。而在氧化傷害(8-OHdG、8-OHdG/Cr)及抗氧化能力方面，不論吸菸、不吸菸族群及所有勞工等在高、中、低三不同暴露組間皆未有顯著之差異。

在肺功能障礙之檢定方面，將肺活量 FVC%＜80%視為異常、FEV1/FVC%＜70%視為異常方面，若依暴露組別之檢定結果顯示(表 10)，高、中、低暴露組各有 1 名異常者，三暴露組間無顯著差異。將 FEV1/FVC%＜70%視為異常，而該變項之正異常百分比分布依暴露組別之檢定，三暴露組間存在顯著差異(p 值=0.0008)；其中高、中、低暴露組各有 9 名(45%)、5 名(14.3%)、0 名(0%)屬於異常。在肺功能障礙分類方面，在三暴露組間之分布(表 11)，高暴露組有 9 名(45%)阻塞型肺功能障礙、1 名(5%)限制型肺功能障礙者，而中暴露組有 5 名(14%)阻塞型肺功能障礙、1 名(3%)限制型肺功能障礙者，低暴露組有 1 名(5%)限制型肺功能障礙者；各不同暴露組間在此分類之分佈表現具顯著差異(p 值=0.002)。

在本研究中，將影響尿中 8-OHdG/Cr 濃度因子依不同累積暴露組別之描述與檢定，結果如表 12 顯示，高暴露組勞工之 8-OHdG/Cr 平均濃度為 5.12±3.32 g/g creatinine、中暴露組勞工為 4.6±3.4 g/g、低暴露組勞工為 5.31±4.08 g/g。將影響尿中 8-OHdG/Cr 濃度之可能因子如年齡、BMI 等納入分層，至於吸菸習慣、吃檳榔習慣之有無及肝功能、肺功能正異常之呈現亦一併納入觀察其各分層勞工之 8-OHdG/Cr 濃度值分佈。不管是各影響因子變項之習慣有無或肝肺功能正異常與否，其分層之 8-OHdG/Cr 濃度值並無顯著差異（除了中暴露組勞工中吸菸習慣與否、低暴露組勞工中吃檳榔習慣與否彼此間有顯著差異存在），而 8-OHdG/Cr 濃度值在各不同暴露組間也是無顯著差異存在。

**三、累積暴露濃度與健康效應之描述及檢定**

本研究將所有勞工之累積暴露濃度與肺功能各變項、氧化傷害等健康效應進行單變相迴歸及相關性之檢定，結果如表 13。可以看出所有勞工之累積暴露濃度與其 FEV1、FEV1%pred、FEV1/FVC%三者肺功能變相間之相關係數及迴歸係數分別

是-0.37、-0.33、-0.63 及-0.03、-0.64、-0.67，且檢定由 p 值顯示皆＜0.05，代表其皆具有意義，累積暴露濃度與 FEV1、FEV1%pred、FEV1/FVC%呈現顯著之負相關。每增加 1 單位的累積暴露濃度 mg/$m^3$*year，則 FEV1、FEV1%pred、FEV1/FVC%顯著減少 0.03L、0.64%、0.67%。而在累積暴露濃度與 FEV1、FEV1%pred、FEV1/FVC%肺功能間之負相關不僅存在所有勞工樣本，而即使區分成吸菸勞工或非吸菸勞工，負相關之情況也相同而且吸菸勞工肺功能減少之程度比非吸菸勞工還多。如以 FEV1 而言，吸菸勞工之 FEV1 隨著累積暴露濃度增加而下降 0.06L，非吸菸勞工下降 0.02L。而至於累積暴露濃度與 FVC、FVC%、8-OHdG、8-OHdG/Cr、TAC 之間則未存有顯著相關性。

## 第二節 肺功能測量、飲食及職場暴露之相關性

因為太多因子會影響肺功能表現，因此除了考慮職場粉塵、游離二氧化矽暴露外，也納入勞工之日用飲食蔬果攝取情形、維他命等抗氧化補充、BMI、抽菸習慣等因子，以了解勞工肺功能、氧化傷害指標及抗氧化能力等相關性。

**一、飲食攝取頻率習慣之影響：**

針對本研究收集之 74 名個案其日用飲食之蔬果等攝取頻率進行問卷調查與分析，無論是深海魚、淡水魚、淡色蔬菜、深綠色蔬菜、胡蘿蔔、番茄、柑橘類水果、柿子、木瓜、芒果、當季水果等隨著飲食頻率而區分為每週≦1 次、每週＞1 次～每天 1 次、每天≧1 次。如表 14 所示，魚類或各類蔬果的攝取頻率並未與體內抗氧化能力達到顯著差異。若進一步進行趨勢檢定，勞工體內抗氧化能力仍未隨著攝取頻率增加而有增加之趨勢。本研究有關胡蘿蔔、番茄、柑橘類水果等攝取頻率與抗氧化趨勢之分佈與先前文獻(Romieu and Trenga, 2001; Aydin et al., 2004)未盡相同，推測應是總樣本數僅 74 名，樣本數太少且也可能存在填寫問卷之回憶誤差。

Schunemann 等調整飲食攝取、吸菸等共變項影響，以複迴歸分析檢定肺功能

與各變項之相關性，觀察到 FEV(1)%、FVC%和黃體素、維他命 C 及 E 的補充有顯著相關性(Schunemann et al., 2001；2002)。一般人若每日攝取抗氧化維他命不當或不足皆易使肺功能下降(Gilliland et al., 2003)，肺功能的表現與水果之攝取量也常存在著劑量-反應之相關性(Kelly et al., 2003)。雖然在本研究中，抗氧化能力與飲食攝取頻率習慣之 ANOVA 分析中，並沒觀察到有顯著差異(表 14)，但將凡有勾選攝取維他命 C、E 或綜合維他命其中一項者則綜稱為具有攝食維他命習慣者，計有 18 名（僅 10 名勞工有攝取維他命 C、5 名勞工有攝取維他命 E、14 名勞工有攝取綜合維他命)。進而由**表 19 複迴歸分析**中，可以看到具有攝食維他命習慣者，其 FEV1 顯著增加 0.38 公升，而 FEV1%pred 之增加則鄰近邊緣值附近（p 值=0.07)。另勞工體內之抗氧化能力亦與 FEV1%pred 呈現正相關，抗氧化能力每增加 1 mmole Trolox/g，則 FEV1%pred 增加 0.15%；而抗氧化能力增加時，FEV1 之增加，則呈現鄰近邊緣值附近（p 值=0.06)。

**二、吸菸因子影響：**

基於吸菸此因子常影響勞工肺功能、氧化傷害之表現，也是導致肺癌、肺炎等肺部相關疾病之危險因子，因此本研究將所有個案區分為吸菸勞工及非吸菸勞工兩組。文獻指出(Repine et al., 1997)，在抽菸者呼吸道上，肺部之抗氧化防衛機制常不足以保護抽菸導致肺部發炎細胞作用下而引起之氧化傷害。但如表 15 所示，在 FEV1，FVC，FEV1%pred、FVC%pred 和 FEV1/FVC%變項上，兩組間並無顯著差異。FEV1 方面，總個案數為 3.09±0.8L，吸菸勞工為 3.22±0.9L，非吸菸勞工為 3.01±0.6L；FVC 方面，總個案數為 3.87±0.8L，吸菸勞工為 4.07 ±1.0L，非吸菸勞工為 3.74 ±0.7L。FEV1%pred 方面，總個案數為 99.49±17.2%，吸菸勞工為 101.66±22.9%，非吸菸勞工為 98.1±12.2%；FVC%pred 方面，總個案數為 105.5±18.8%，吸菸勞工為 109.95±23.3%，非吸菸勞工為 102.65±14.7%；FEV1/FVC%方面，總個案數為 79.82±10.7%，吸菸勞工為 78.39±12%，非吸菸勞工為 80.75±9.9%。因為本研究案之總個案數為 74 名，而有吸菸習慣者佔 29 名，

可能有吸菸暴露與對照之樣本數不夠大也比較不易看出兩者之差異。而由**表 19 複迴歸分析**中，可以看到具有吸菸習慣者，其 FEV1/ FVC%顯著比未吸菸勞工少 4.57%，但 FVC 反而增加。

即使在氧化傷害（8-OHdG 和 8-OHdG/crea）方面，吸菸勞工與非吸菸勞工兩者間亦無顯著差異。尿中 8-OHdG 方面，吸菸勞工為 16.8±35.2ng/ml，非吸菸勞工為 10.32±9.8ng/ml；8-OHdG/crea 方面，總個案數為 4.9±3.5μg/g，吸菸勞工為 5.02±3.6μg/g，非吸菸勞工為 4.85±3.5μg/g。至於抗氧化能力方面，所有勞工總個案數、吸菸勞工、非吸菸勞工分別為 65.16±30.6、68.36±32.4 及 63.09±25.6 mmole Trolox/g，吸菸勞工與非吸菸勞工兩者間亦無顯著差異。Berg 等研究結果顯示，蔬果量攝取較多者，其血液中之維他命濃度及抗氧化能力皆較高，但尚不足以造成脂質及 DNA 氧化傷害的保護效果，所以其血液中有關氧化傷害之生物效應指標並未有明顯差異(van den Berg et al., 2001)。而如表 14 所示，本研究觀察勞工雖隨著各項蔬果、魚類飲食頻率不同但體內抗氧化能力並未有顯著差異變化。在本研究中，將 8-OHdG 與抗氧化能力指標進行單變相迴歸分析中，其迴歸係數為-0.8，但 p 值僅為 0.45(表 18)。

**三、BMI 因子影響：**

有關國人體胖區分方面，依據衛生署先前區分為 BMI：18～24 屬於正常、24≤BMI<27（過重）和 BMI≥27（肥胖），身體質量指數正常者有 27 名、過重者有 27 名、肥胖者有 20 名（表 16）。因此本研究依此 BMI 分類觀察肺功能各變項、8-OHdG/crea 及抗氧化能力與 BMI 之關係，由表 16 可知，肺功能各變項、8-OHdG/crea 及抗氧化能力與 BMI 分組間並未有顯著差異（僅 FVC 該變項和 BMI 分類之關係達邊緣值附近，p 值=0.09）；但進一步趨勢檢定方面，可看出 FEV1、FVC、FVC%pred 在身體肥胖 BMI 分組上，隨著身體質量指數增加有顯著的減少；趨勢檢定之 p 值分別為 0.018、0.018、0.036。此可印證先前文獻研究中，特別是一般過重及肥胖民眾，其 BMI 和肺功能兩者間呈現線性負相關(Bua et al., 2005; Chinn

et al., 2005)，其主要原因大多因為較肥胖者，其腹肋膜間接影響肺功能。且這樣之負相關情況，男性比女性表現更明顯(Harik-Khan et al., 2001)，即使是求學學齡之孩子也是相同情況(Chu et al., 2009)；而本研究案所收集之個案皆限定為鑄造業男性勞工。而在抗氧化能力與 BMI 分組間之趨勢檢定方面，其隨著身體質量指數增加有顯著之增加。雖然肥胖對肺功能有不好影響，但有少數研究利用 BMI 來監控肺部病人營養攝取等治療之復原情況，而當其 BMI 上升時其肺功能同時改善(Pedreira et al., 2005; Vibhuti et al., 2007)。但針對本研究之 14 名有肺功能障礙者分析，並未發現到 BMI 和各肺功能變項間存有任何相關性。

**四、職場粉塵累積暴露之影響：**

本研究將每位勞工之粉塵暴露濃度乘上其於本廠之工作年資視同其累積暴露濃度，而為了解職場粉塵等累積暴露濃度與肺功能各變項、8-OHdG/crea 及抗氧化能力關係，進行暴露量分組間之差異分析及趨勢檢定。將所有 74 名勞工暴露量之分佈分組，由表 17 結果顯示，肺功能之變項 FEV1、FEV1%pred、FEV1/FVC%在累積暴露濃度分組上具有明顯之差異；其 p 值分別為 0.005、0.01、0.0002。並且趨勢檢定方面，可以看出 FEV1、FEV1%pred、FEV1/FVC%在累積暴露濃度分組上，隨著累積暴露濃度增加有顯著的減少；其 p 值分別為 0.002、0.003、＜0.0001。而 8-OHdG/crea 方面，在累積暴露量分組間及趨勢檢定方面皆未有顯著差異。Pilger et al.(2000)曾指出罹患矽肺症病人尿中 8-OHdG 濃度與 FEV1%、FVC%有顯著正相關；乃因體內 8-OHdG 形成與修補能力無法達成平衡，而使氧化 DNA 傷害之修補能力下降所致。本案進而將 8-OHdG/Cr 與 FEV1%pred、FVC%pred、FEV1/FVC%進行單變項迴歸分析中，其迴歸係數分別為 0.73、0.45、0.55，雖是正相關，但皆未達顯著意義。另外亦將 8-OHdG 濃度與累積暴露量進行單變項迴歸分析，其迴歸係數為-0.04，而 p 值僅為 0.4(表 18)。至於本案勞工之 8-OHdG/crea 是否也類似因其氧化 DNA 傷害之修補能力下降而致使累積暴露濃度增加而其濃度卻減少，則須納入更多因子討論或校正後方能定論。

為進一步探討肺功能與其他變項之共同影響，我們進行了 FEV1，FVC，FEV1%pred，FVC%pred 和 FEV1/FVC%各變項與年齡、BMI、吸菸、累積暴露濃度、抗氧化能力與維他命攝取之**複迴歸分析**。結果如表 19 顯示，FEV1 隨著年齡(p 值=0.003)、BMI(p 值=0.003)、累積暴露濃度(p 值=0.04)的增加而有顯著的減少，而隨著有攝食維他命習慣而 FEV1 亦增加(p 值=0.05 邊緣值)。FVC 隨著年齡(p 值=0.01)、BMI(p 值=0.006)的增加而顯著的減少，但有吸菸習慣者 FVC 竟不同以往研究結果反而增加。FEV1%pred 隨著 BMI(p 值=0.0003)、累積暴露濃度(p 值=0.0009)的增加而有顯著的減少，而隨著抗氧化能力增加(p 值=0.01)而顯著的增加；另亦隨著攝食維他命習慣而增加（p 值=0.07，邊緣值附近）。FVC%pred 隨著 BMI 的增加而有顯著的減少(p 值=0.004)；FEV1/FVC%變項則隨著有吸菸習慣(p 值=0.03)、累積暴露濃度的增加(p 值＜0.0001)而有顯著的減少。整體而言，至於 FEV1，FVC 如預期隨著年齡增長而衰減(p 值分別為 0.003、0.01)，而 BMI 顯著影響了 FEV1、FVC、FEV1%pred、FVC%pred 之呈現，可印證文獻之肥胖程度顯著讓肺功能下降。而累積暴露濃度顯著影響了 FEV1、FEV1%pred、FEV1/FVC%之呈現，也印證文獻之鑄造業勞工暴露量越多顯著讓肺功能下降。且勞工體內之抗氧化能力增加其 FEV1%pred 表現(p 值=0.01)，而 FEV1、FEV1/FVC%之增加則鄰近邊緣值附近(p 值皆為 0.06)。具有攝食維他命習慣者，其 FEV1 也增加(p 值=0.05)，而 FEV1%pred 之增加則鄰近邊緣值附近(p 值=0.07)。因此本研究強調 BMI、累積暴露濃度皆和肺功能呈現負相關之關係。即 BMI 每增加 1 $kg/m^2$ ，將導致 FEV1 下降 0.08L、FVC 下降 0.09L、FEV1%pred 下降 2.48 %、FVC%pred 下降 2.34 %。而累積暴露濃度每增加 1 $mg/m^3$*year，將導致 FEV1 下降 0.02L、FEV1%pred 下降 0.77%、FEV1/FVC%下降 0.66%。

由於本研究結果顯示，不論是針對該 74 名鑄造業勞工或是其中肺功能健康之 56 名勞工進行趨勢檢定，檢定結果皆是如同表 16、表 17 之結果所示，隨著職場粉塵暴露增加及個人 BMI 之增加，其肺功能皆呈現減少之趨勢。因此本研究進而

針對作業環境粉塵濃度較高之A廠實施工程介入，利用水霧減少粉塵暴露。

## 第三節 A鑄造廠實際現場改善

本計畫之實際現場改善與工研院合作，由工研院鑄造業輔導小組針對A廠進行現場工程改善。其主要針對高粉塵暴露之作業區，拆模機、集塵設備、廢砂推放區，採取噴水霧裝置(如圖3~5)，並針對大型鑄件之拆模機，配合起重機動線規劃具簾幕效果之水霧。水霧系統高度為3公尺高，其在拆模機部份；以不妨礙上方天車進入軌道之原則下來設計在鑄件進出的開口面建構水務系統；另同時該水霧系統亦涵蓋廢砂堆放區。一般鑄造廠作業基於安全考量，常禁止水之存在，因此本研究採取水滴粒徑小之水霧系統，並遠離澆鑄區及炙熱之鑄件區，而設置於已稍冷卻鑄件之拆模區。該水霧系統規格為：1.噴頭，孔徑：0.3m/m、出水量：110 ml/min，共計100個噴水孔。2.馬達，工作壓力：50～70kg/$cm^2$、出水量：5 L/min，共計2台馬達。此工程改善設備，開啟使用及未開啟情形很清楚顯示於圖5，其主要目的在於控制拆模機粉塵逸散、藉助水霧以減少拆模區揚塵。除水霧裝置外，而另於4公尺高度處亦設置2台直徑1.2公尺之換氣壁扇(圖3、圖4)裝置，以此整體換氣裝置導引其他區域乾淨空氣導進入拆模區，以期降低現場作業人員暴露量。

工研院特地委請另外1家認證機構進行現場採樣分析，以評估改善成效；A廠改善前後之現場總粉塵及可呼吸性粉塵分布情形如圖4所示。本研究針對該廠拆模區附近進行改善前、後作業環境中可呼吸性粉塵及游離二氧化矽之採樣及分析，該鑄造廠改善前、後之可呼吸性粉塵濃度分別為2.87±1.38 mg/$m^3$、1.60±0.70 mg/$m^3$，如表21所示；前後濃度差異p值在邊緣值附近(p=0.07 Wilcoxon sign rank test)。而改善前、後之可呼吸性游離二氧化矽濃度分別為0.43±0.25 mg/$m^3$、0.18±0.11 mg/$m^3$；前後濃度明顯差異(p<0.05 Wilcoxon sign rank test)。雖然本研究只針對該廠拆模區附近進行水霧工程等改善，但因為該鑄造廠廠區內部各不同

製程間並未進行硬體牆壁等空間實體隔間，所以整體廠區在高粉塵暴露之拆模區進行局部區域實際現場改善後全廠之粉塵暴露已經下降。而基於如此之結果促使可呼吸性粉塵濃度在改善後降低44%(2.87 ± 1.38mg/$m^3$ 降為 1.60 ± 0.70 mg/$m^3$)，可呼吸性游離二氧化矽濃度在改善後則降低58%(0.43 ± 0.25mg/$m^3$ 降為 0.18 ± 0.11mg/$m^3$)；顯示利用水霧系統改善鑄造廠之作業現場是可以有效的控制勞工粉塵暴露。

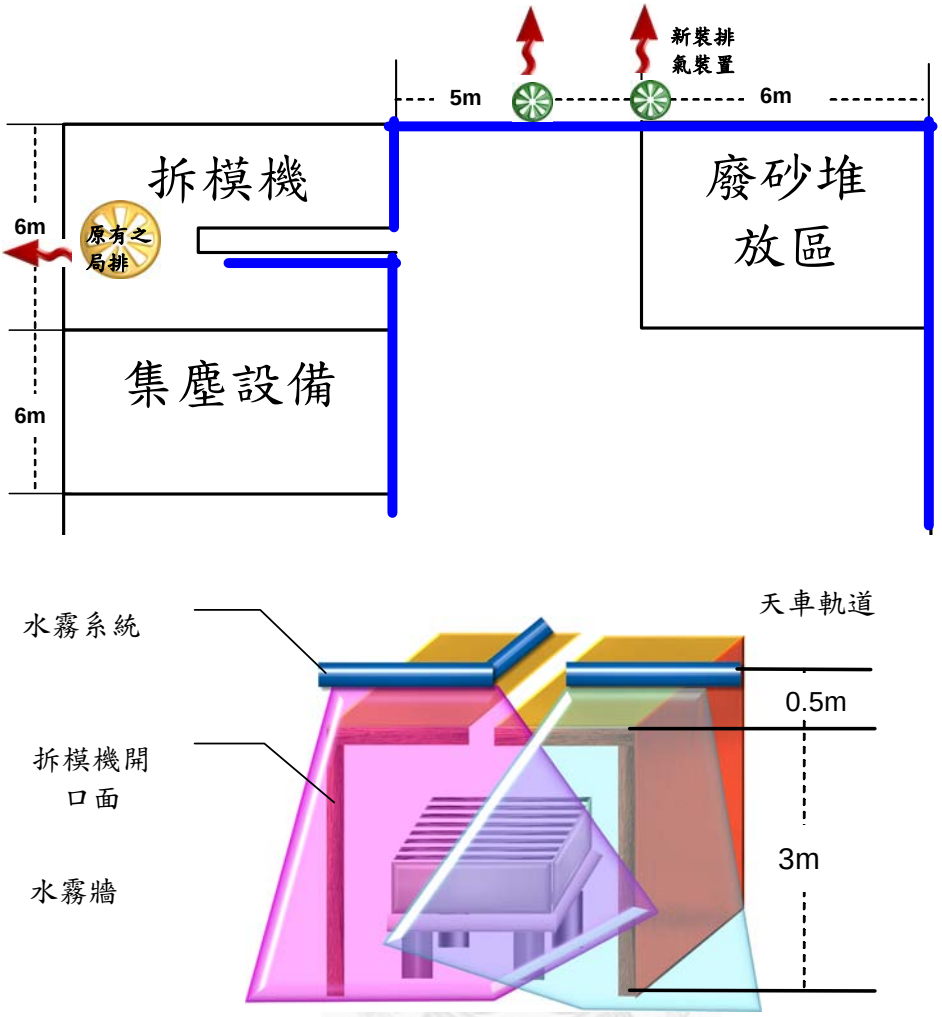



圖 3 工程改善廠區規劃及水霧裝置圖

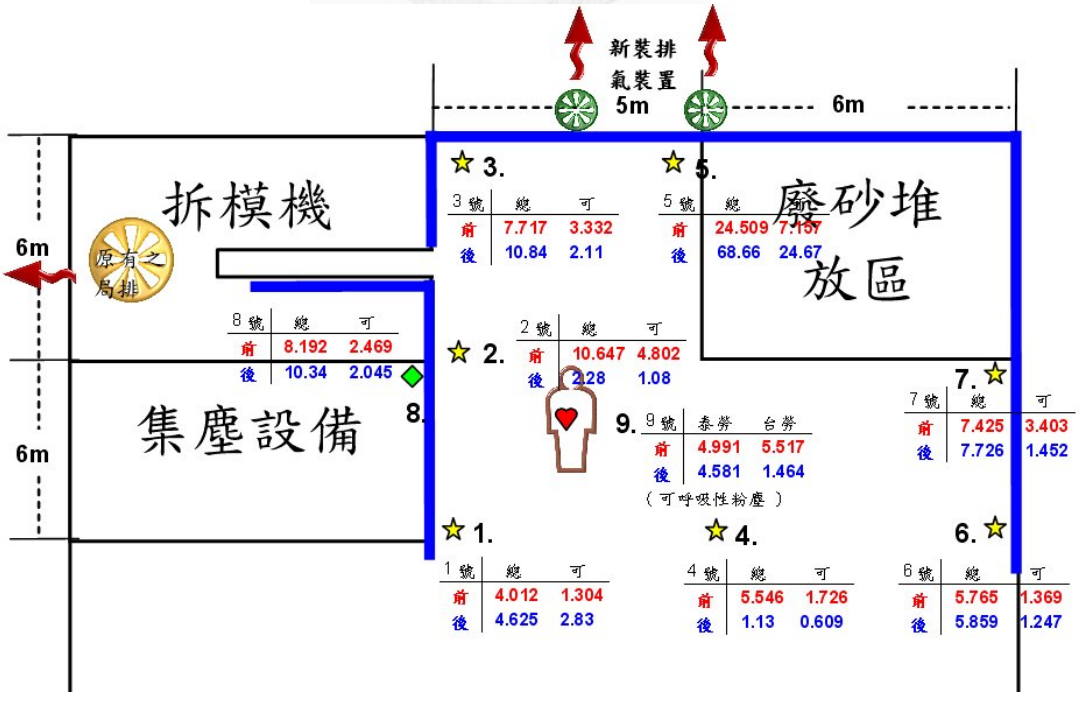



圖 4 A 廠改善前後之現場總粉塵及可呼吸性粉塵分布情形

**未開起水霧及排氣裝置現況**

**整體換氣裝置與水霧開啟時現況**

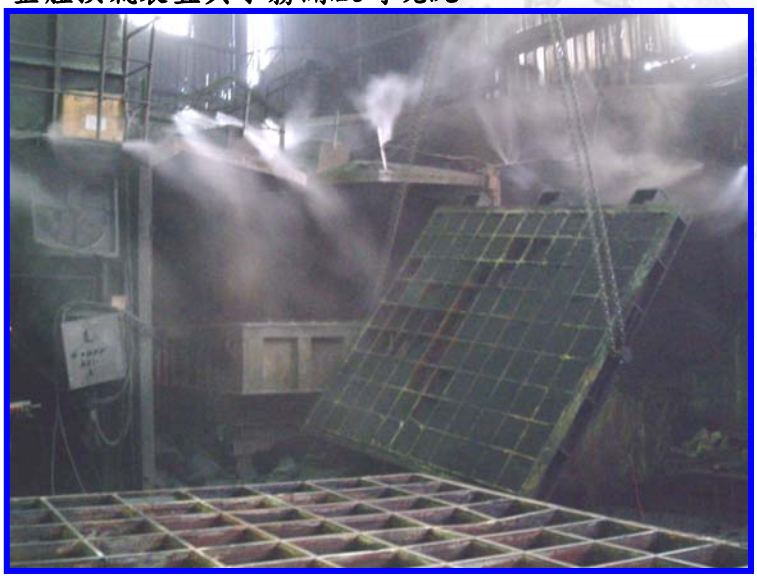


圖 5　水霧開啟使用前後情形圖

## 第四節 作業環境改善與生物性指標之變化

本案共計收集有 A 廠 22 名男性勞工納入作業環境改善之健康追蹤，其年齡平均為 44.3 歲 (SD 11.2)，平均工作年資為 13.3 年 (SD 18.3)，工作類別以合模(41%)及造模(45%)居多，過半數勞工現為吸菸者(55%)。而在胸部 X 光檢查方面，

有 5 名依 ILO 判讀標準診斷隸屬為 1/0、2 名診斷為 1/1，其餘 15 名為健康狀況(0/0)(如表 20)。

**一、肺功能改善：**

A 廠勞工在經歷作業環境現場改善三個月後進行肺功能及尿中 8-OHdG 的健康追蹤，在肺功能方面，整體勞工平均上其有明顯的改進，但吸菸勞工其尿中 8-OHdG 濃度卻也增加。如表 21 所示，該廠整體勞工及非吸菸組勞工之肺功能 FEV1，FVC，FEV1%pred、FVC%pred 在三個月後皆有顯著增加，其 p 值皆小於 0.05；而 FEV1/FVC%則沒有顯著差異。肺功能改善方面，可以看到非吸菸勞工其 FEV1 增加 28.6%、FVC 增加 30.0%, 、FEV1 %pred 增加 31.1%、FVC %pred 增加 30.9%，而吸菸勞工其 FEV1 %pred 增加 25.0%、FVC %pred 增加 24.0%。由於吸菸勞工在 FEV1、FVC(p 值介於邊緣 0.059)並未像整體勞工及非吸菸組勞工在改善後有顯著差異，因此推測吸菸該變項應是一干擾因子導致。而根據先前郭等針對台灣中部鑄造廠進行肺功能與暴露之健康調查，結果顯示粉塵累積暴露濃度越高其肺功能情況越差，罹患矽肺症之風險則越高(Kuo et al.,1999)。此部份可以佐證本研究工程改善之重要性，且該廠勞工在工程改善前，計有 17 名勞工肺功能正常、3 名有阻塞型肺功能障礙、2 名有侷限型肺功能障礙(表 20)；工程改善後，計有 20 名勞工肺功能正常、2 名有阻塞型肺功能障礙。

本研究針對肺功能、尿中 8-OHdG、粉塵累積暴露及工程介入改善進行 GEE 檢定，同時亦進行年齡、BMI、吸菸等干擾因子校正，結果如表 22。如預期一般，FEV1 和 FVC 數值隨著年齡增加而遞減，而 FEV1，FVC， FEV1%pred、FVC%pred 該四項肺功能變項隨著改善介入而前後有顯著增加；logFEV1 增加 0.103L、logFVC 增加 0.106L、 logFEV1%pred 增加 0.104L、logFVC%pred 則增加 0.106L。而胸部 X 光結果方面，ILO 1/0 比 category 0/0 之 FEV1/FVC%有顯著較低(p=0.02)。Porter(2006)等其研究更指出，即使停止游離二氧化矽暴露後，游離二氧化矽持續作用導致肺部產生之氧化氮、ROS 仍持續增加，以至於後續仍產生嚴重之氧化傷

害；Scabilloni 等(2005)之動物實驗結果也指出停止游離二氧化矽暴露後肺部纖維化持續進行。而根據 Gamble et al.(2004)針對矽肺症與肺功能之相關性探討，該文獻指出當矽肺症判讀為 ILO 1/1、ILO 0/0 這兩者間之肺功能差異很難區別開來，而當 ILO 3/3 時，因為肺纖維結節將使肺功能明顯下降。因此可知，肺功能變化與胸部 X 光判讀之塵肺症等級有很大關係；而在本研究中，改善前 22 名勞工中僅有 2 名判讀可能具有塵肺症(ILO 1/1)、5 名判讀 ILO 1/0（表 20）。因此推測本研究個案因為職場游離二氧化矽暴露所導致之肺部傷害皆屬於初期症狀，尚未嚴重至肺纖維結節，因此在暴露初期及早工程介入，對於肺功能提升及降低後續之氧化傷害皆大有助益。

**二、8-羥基去氧鳥糞核苷健康追蹤：**

至於尿中 8-OHdG 及 8-OHdG/Cr 的健康追蹤與檢定，在非吸菸勞工部份，改善前後並無顯著差異；在吸菸勞工部分及所有勞工個案，僅 8-OHdG/Cr 該項於改善前後呈現顯著差異(表 21)。而在 GEE 檢定方面，本研究顯示尿中 log 8-OHdG/Cr 在改善介入後增加 0.77$\mu$g/g 之變化呈現在邊緣值附近(p=0.08），如表 22。

由於吸入含游離二氧化矽之粉塵將導致氧化壓力進而傷害肺部(Ding et al. 2002; Fubini and Hubbard 2003; Orman et al. 2005)，在正常情況下體內受到氧化性傷害與修補的速率會達到平衡，如果在尿中發現有較高的 8-OHdG 濃度，表示體內氧化性傷害也相對較大，因為在修補切除殘基後將水溶性 8-OHdG 代謝至尿中，通常職業暴露越嚴重，勞工其尿中 8-OHdG 濃度越高。

根據 Porter 等(2002， 2006)針對游離二氧化矽暴露與氧化氮、ROS 產生之相關性所進行之研究，皆顯示老鼠經游離二氧化矽暴露後，其氧化壓力引起之肺部傷害較嚴重。而 Knaapen et al(2002)利用老鼠動物實驗及 Schins et al(2002)培養 A549 細胞株，其在游離二氧化矽暴露下亦呈現 DNA 傷害之相似研究結果，而且暴露量越高，氧化傷害越嚴重，導致尿中 8-OHdG 濃度亦增加，所以尿中 8-OHdG 濃度與工作期間長短有關。Fubini 和 Hubbard( 2003)也指出游離二氧化矽暴露

將持續產生 ROS、氧化傷害導致肺泡細胞持續發炎。但尿中 8-OHdG 濃度除反應暴露情形外，也會與個人 DNA 修補能力有關，Halliwell(2000)指出體內 8-OHdG 濃度只能代表氧化傷害之形成與修補能力兩者間之平衡狀況，因此外來之暴露也可能刺激 DNA 傷害之修補能力而使 8-OHdG 濃度下降。而 Pilger et al.(2000)先前研究比較 42 名得矽肺病之已退休之人員與 63 名暴露石英之作業人員兩個群體之氧化性傷害與肺功能之關係，亦曾指出罹患矽肺症病人因生理因素導致體內 8-OHdG 形成與修補能力無法達成平衡，使氧化 DNA 傷害之修補能力下降，因此尿中 8-OHdG 濃度與 FEV1.0%、FVC%有顯著正相關；此結果與本研究改善後勞工肺功能增加、8-OHdG 濃度亦增加之結果相似。尿中 8-OHdG 可以經過三個來源：1.受氧化傷害 DNA 修補產物、2.從核苷酸受氧化之 dG 移除、3.細胞轉換變動(turnover)，這意味尿中 8-OHdG 代表全身 DNA 氧化傷害之平均濃度。而且 DNA 的氧化傷害除了職場暴露影響外，也受吸菸等各因子相互作用的影響(Mukherjee et al. 2004)；在本研究中，吸菸勞工之尿中 8-OHdG/Cr 在介入改善後反而增加，也可能是吸菸與 DNA 傷害之修補能力相互作用所導致。

一般體內 8-OHdG 濃度可代表環境暴露之生物有效標記，但其受許多因素影響；文獻中常提及之因素為吸菸、年齡、BMI、飲酒、運動、營養品補充、職業暴露及嚼檳榔等(整理歸納如表 2)，而職業暴露亦包括有諸多化學污染物質（游離二氧化矽、重金屬、硫氧氮化物、多環芳香烴或苯等等），甚至個人基因多型性差異影響 8-OHdG 代謝(Gromadzinska and Wasowicz 2003)等因素皆未納入本研究之量測，此為本研究之研究限制。

## 第五節 B 鑄造廠 DNA 損傷、免疫毒性及職場暴露之相關分析

本研究中使用彗星試驗去評估 B 鑄造廠 27 位勞工中游離二氧化矽對其 DNA 造成的傷害，藉以瞭解基因毒性；並針對各勞工血液中六種細胞激素進行分析，分別為介白素-2(IL-2)、介白素-4 (IL-4)、介白素-6(IL-6) 、介白素-10(IL -10)、

干擾素-γ(IFN-gamma)、腫瘤壞死因子(TNF)，進而將職場暴露狀況一併納入考量，觀察游離二氧化矽暴露與該廠勞工 DNA 損傷、免疫毒性之相關性。

**一、彗星分析與 DNA 損傷程度**

參與 DNA 損傷、免疫毒性檢測之 B 鑄造廠 27 位勞工中，基本人口學變項如表 23，有 20 名勞工≧50 歲、28 名 BMI(kg/m$^2$)≧24、25 名勞工為閩南人、16 名教育程度為國中以上、25 名勞工已婚；大部分勞工沒有吸菸、嚼檳榔、喝酒習慣（分別為 17、20、15 名)，而大部分勞工有運動習慣(20 名)及於職場中攜帶防護具習慣(25 名)。B 鑄造廠比起其他 A、C 兩廠而言，屬於年齡較大、工作年資較長者(見表 5)。本次研究中採取了四個參數(頭尾比例、尾部長度、尾部動量、Oliver 尾矩)作為 DNA 傷害程度之結果，所有 B 廠勞工之頭尾比例平均為 7.75±1.28、尾部長度平均為 287.43±61.23、尾部動量平均為 184.75±59.19、Oliver 尾矩平均為 75.7±31.1。而此四個參數在基本人口各變項之分層方面，不論是年齡、BMI、籍貫、教育程度、婚姻狀況、吸菸、嚼檳榔、喝酒、運動、攜帶防護具等不同組別間皆無顯著差異(表 23)。

在 1993 年一篇關於結晶型二氧化矽造成 DNA 氧化性傷害的文獻說明在持續的時間內(3 星期)暴露高濃度(30mg/ml)的二氧化矽會造成 DNA 鏈斷裂(Daniel et al., 1993)。在 2001 年，Seiler 等人在動物實驗中發現 Ki-67 老鼠的細胞只有在暴露 1.5mg 和 7.5mg 石英後，肺部細胞 DNA 的 8-oxoGua 才會顯著增加，暴露 0.3mg 的石英則沒有顯著增加，8-oxoGua 也是一個 DNA 受到損傷之指標，在此篇中石英暴露對 DNA 傷害程度並未發現劑量-反應之關係，表示應暴露一定劑量後才會發現 DNA 有顯著傷害之情形(Seiler et al., 2001)。而在 2003 年一篇關於陶瓷廠與鑄造廠的研究中提及，經年齡、吸菸習慣等因子校正後暴露二氧化矽之員工比未暴露到二氧化矽的健康人發現 DNA 傷害比較嚴重(Basaran et al., 2003)。之前 Lee 等針對 Extent tail moment、Tail DNA%、Tail length 三種尾部指標去做探討，觀察暴露組與對照組兩組中之淋巴細胞、T 細胞、B 細胞以及 G 細胞，以 Tail length

為 DNA 傷害指標，發現在這四種細胞中都可以看到 DNA 傷害程度在暴露與對照兩組間有顯著差異(p<0.0001)，其他三種指標則沒有(Lee et al., 2004)。

而本研究為了解該廠勞工游離二氧化矽累積暴露量與 DNA 損傷之相關性，進行累積暴露量與 DNA 傷害四參數之單變項迴歸分析，結果如表 24 顯示，p 值皆大於 0.05，未具有統計上意義。但在控制一些干擾因子後，如年齡、籍貫、教育程度、吸菸情形及維他命 E 使用情形等，可以清楚看出累積暴露量與 DNA 傷害四參數具有統計上顯著意義(表 25)；如游離二氧化矽累積暴露量每增加 1 mg/$m^3$*year，將導致頭尾比例增加 0.59(p 值=0.04)、尾部長度增加 0.76(p 值=0.009)、尾部動量增加 0.84(p 值=0.004)、Oliver 尾矩增加 0.78(p 值=0.009)。因此認為頭尾比例、尾部長度、尾部動量、Oliver 尾矩在本研究中可以當作游離二氧化矽暴露造成勞工 DNA 傷害情形之指標。

**二、細胞激素與免疫毒性**

本研究針對六種細胞激素進行分析，分別為介白素-2(IL-2), 介白素-4 (IL-4), 介白素-6(IL-6) , 介白素-10(IL -10) , 腫瘤壞死因子(TNF), 干擾素-γ (IFN-γ )。所有 B 廠勞工之 IL-2 平均為 10.7±27.3、IL-4 為 1.72±1.04、IL-6 平均為 2.36±1.84、IL -10 平均為 1.96±0.99、TNF 平均為 1.47±0.98、IFN-γ 平均為 6.04±7 pg/ml(表 26)。而此六種細胞激素在基本人口各變項之分層方面，不論是年齡、BMI、籍貫、教育程度、婚姻狀況、吸菸、嚼檳榔、喝酒、運動、攜帶防護具等不同組別間大都無顯著差異；然 IL-4 在年齡分組上有顯著差異(p 值=0.02) ，另 IL-4 在籍貫分組以及 IFN-γ 在教育程度、攜帶防護具分組間的比較，接近統計上顯著意義(p 值分別為 0.06、0.09、0.06) (表 26)。

當游離二氧化矽進入人體內，會活化T細胞產生Th1及Th2免疫反應，與Th1免疫反應相關的細胞激素有IFN-γ和IL-2，與Th2免疫反應相關之細胞激素則有IL-4, IL-6, IL-10等，IFN-γ與IL-4會影響巨噬細胞而產生TNF，TNF則是發炎反應中的一個相關因子，然而其他的細胞激素也似乎占了一定影響。體內細胞激素會被外來物質所刺激，二氧化矽刺激將會活化T細胞而引起Th2型免疫反應，而矽肺

症發生與發炎反應息息相關，Th2型免疫與發炎反應有相關。體內細胞激素會被外來物質所刺激，游離二氧化矽刺激將會活化T細胞而引起Th2型免疫反應，而矽肺症發生與發炎反應息息相關，Th2型免疫與發炎反應有相關。

在2007年關於從事水泥磚瓦學員體內細胞激素與免疫反應之研究說明這些學員暴露到高濃度含游離二氧化矽的粉塵，其體內 IL-1$\beta$, IL-2, IL-4, IL-10 與 IFN-$\gamma$ 濃度顯著比電器工人高(Carlsten et al., 2007)。而 2005 年的一個研究說明表現在暴露到游離二氧化矽之老鼠體內細胞激素 IL-4 有增加的趨勢(Chen et al., 2005)，IL-4 是屬於 Th2 的免疫反應，目前較多關於細胞激素研究都以體外試驗或活體試驗為主，可能因為人體內細胞激素會受到的影響因子較多。另外在 2002 年有一篇針對人類嗜鹼性細胞暴露到柴油引擎燃燒所生成之微粒後，發現 IL-4 有增加之情形(Devouassoux et al., 2002)。在 2004 年的一個研究發現 RAW 264.7 老鼠巨噬細胞以不同濃度的二氧化矽做處理，發現二氧化矽濃度越高，TNF-$\alpha$與 IL-6 的濃度會越高，且有劑量-反應關係(Balduzzi et al., 2004)。在 2000 年一篇研究針對人類上皮肺細胞(A549)暴露到礦物性微粒，如石英、綠簾石等會造成 IL-6 及 TNF 之上升(Hetland et al., 2000)。而 IL-10 則是屬於一種多功能型的的細胞激素，雖被定義為 Th2 型免疫反應細胞激素，但近年來發現 IL-10 擁有強烈的抗發炎效應。有研究發現 IL-10 過度的表現會增加肺部纖維化以及二氧化矽會引起 IL-10 的 Th2 型免疫反應(Barbarin et al., 2005)。

而本研究為了解該廠勞工游離二氧化矽累積暴露量與各細胞激素之相關性，進行累積暴露量與免疫反應六種細胞激素之單變項迴歸分析，結果如表 27 顯示。除 IFN-$\gamma$之迴歸係數 0.42，接近統計上顯著意義(p 值=0.06)；其餘 p 值皆＞0.05，未具有統計上意義。

但為探討 B 廠勞工各影響因子與細胞激素之相關，在複迴歸分析，將年齡、籍貫、吸菸情形、BMI 及是否罹患矽肺症等因子納入模式中，如表 28，可以清楚看出 IL-2 與是否罹患矽肺症具有統計上顯著意義(p 值＝0.04)；即罹患矽肺症(含 1/0 以上)之勞工比沒罹患矽肺症之勞工還有較多 1.13 之 LogIL-2 pg/ml。IL-10

與是否罹患矽肺症該變項亦具有統計上顯著意義(p 值＝0.01)，罹患矽肺症(含 1/0 以上)之勞工比沒罹患矽肺症之勞工還有較多 0.46 之 LogIL-10 pg/ml。

# 第五章 結論與建議

本研究以 74 位鑄造業勞工為對象進行橫斷性研究：了解其肺功能與飲食攝取、氧化傷害、抗氧化能力指標、BMI、職場暴露等相關性。結果發現，肺功能 FEV1，FEV1%pred、FEV1/FVC%與職場粉塵累積暴露濃度、BMI 等趨勢分佈皆有顯著之負相關。且所有勞工之累積暴露濃度與其 FEV1、FEV1%pred、FEV1/FVC%三者肺功能變項間之相關係數及迴歸係數分別是-0.37、-0.33、-0.63 及-0.03、-0.64、-0.67，且檢定由 p 值顯示皆小於 0.05，代表其皆具有統計上意義。

針對 B 鑄造廠 27 位勞工 DNA 損傷、免疫毒性及職場暴露之分析結果發現，在控制一些干擾因子後，如年齡、籍貫、教育程度、吸菸情形及維他命 E 使用情形等，累積暴露量與 DNA 傷害四參數（頭尾比例、尾部長度、尾部動量、Oliver 尾矩）皆具有統計上顯著意義。至於細胞激素分佈方面，將年齡、籍貫、吸菸情形、BMI 及是否罹患矽肺症等因子納入複迴歸分析模式中，可以了解罹患矽肺症(含 1/0 以上)之勞工比沒罹患矽肺症之勞工有較多 IL-2、IL-10。

另針對 A 廠以實際工程改善介入勞工工作現場，探討改善後三個月肺功能及 8-OHdG 生物指標變化之縱斷性研究，其結果顯示，肺功能指標 FEV1、FVC、FEV1%pred、FVC%pred 在作業環境改善後有明顯的增加，並達統計顯著差異。

本研究有關勞工體內抗氧化能力並未隨著攝取抗氧化蔬果頻率增加而有增加之趨勢，推測因總樣本數僅 74 名，樣本數較少，且也可能存在填寫問卷之回憶誤差；故後續應擴充樣本數以釐清飲食、氧化傷害及抗氧化之關係。另外本研究之生物指標，如體內 8-OHdG 濃度及肺功能並非專一性代表游離二氧化矽之暴露，其受許多因素影響，如：吸菸、年齡、BMI、飲酒、運動、營養品補充、職業暴露及嚼檳榔等，而職業暴露亦包括諸多化學污染物質（游離二氧化矽、重金屬、硫氧氮化物、多環芳香烴或苯等等），甚至個人基因多型性差異亦可影響 8-OHdG 代謝，然這些因素因採樣工廠配合意願不高故皆未納入本研究之量測，此為本研究之研究限制。而在生物指標方面，因為 8-OHdG 半衰期約 6~8 小時，屬於非長期暴露累

積效應之指標，故在此次改善前後之變化並不顯著。日後相關研究除了環境測定納入重金屬、多環芳香烴等諸多化學污染物質以外，建議可於問卷設計時將勞工是否於工作現場吸菸、吸菸量之根數等、進入鑄造廠前之相關暴露史、鑄造工廠先前之環境測定資料（國內一般常以厭惡性粉塵看待，並無游離二氧化矽之環測值）等等皆納入收集範疇中。

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表 1 游離二氧化矽之流行病學研究

| 研究者，國家 | 世代族群 | 病例* | 可呼吸性粉塵之游離二氧化矽含量 | 評估方式 |
|---|---|---|---|---|
| Hnizdo and Sluis-Cremer (1993), 南非, 世代研究 | 2,235 位 45~54 歲地下金礦白人男曠工，收集 1968~1971 年之健檢資料。個案包括 1938 年後開始納入工作年數，且年資超過 10 年，追蹤至 1991 年。 | ILO category ≥ 1/1 (313 個案) | 30% | 累積風險 |
| Hughes et al. (1995), 美國, 回溯性世代研究 | 2,342 位矽藻土白人男礦工，1942~1987 年間至少工作一年以上。 | 1809 位實際參加胸部 X 光檢查，ILO category ≥1/0 (81 個案) | 3%～60% | 累積風險 |
| Kreiss and Zhen (1996), 美國, 礦工及社區區民 | 134 個案，其中 34 位在 hardrock 礦區附近城市無職業暴露、40 歲以上之男居民當對照組， 另暴露組為 100 位 有游離二氧化矽暴露之 hardrock 礦工(包括 32 矽肺症個案) | ILO category ≥1/0 | 12.3% | 盛行率 |
| Muir et al. (1989), Muir(1991); 加拿大，回溯性世代研究 | 2,109 位 Ontario 金礦及釉礦勞工，1940~1959 年間至少工作五年以上，追蹤至 1982 年。 | ILO category ≥ 1/1 | 6.0% (金礦)及 8.4%(釉礦) | 累積風險 |
| Ng and Chan (1994), 香港, 橫斷式研究 | 338 位勞工，1967~1985 年間至少工作一年以上。 | ILO category ≥ 1/1 | 27% | 盛行率 |

| | | | | |
|---|---|---|---|---|
| Rosenman et al.(1996), 美國,橫斷式研究 | 1072 位鑄鐵廠勞工（含 549 現職, 497 退休, 26 離職）。 | ILO category ≥ 1/0 | -- | 盛行率 |
| Steenland and Brown (1995), 美國,世代研究 | 3,330 位金礦白人男曠工，1940~1965 年間至少工作一年以上，追蹤至 1990 年。 | ILO category ≥ 1/1 或死亡 | 13% | 累積風險 |

*：ILO 針對塵肺症患者將其區分為 category 0：0/-, 0/0, 0/1、category 1：1/0, 1/1, 1/2、category 2 : 2/1, 2/2, 2/3、category 3 :3/2, 3/3, 3/+

表 2　各不同研究中影響 8-OHdG 之因素整理表

| 文獻作者年代 | 族群(n) | 8-OHdG | 吸菸 | AGE | BMI | 飲酒 | 運動 | 營養品 | 職業暴露 | 其他 |
|---|---|---|---|---|---|---|---|---|---|---|
| Feng et al.(2006)美國 | 一般吸菸男性(110) | 尿液，LC-MS/MS | △ | △ | △ | | | | | |
| Huang et al.(2000)美國 | 健康男性(80)<br>健康女性(100)<br>全部為非吸菸者 | 尿液，ELISA | | △ | △ | △ | － | baseline<br>每日蔬果攝取(－)<br>血清中維生素 C(－)<br>營養品補充(－)<br>服用 2 個月 Vit.C(△)<br>服用 2 個月 Vit.E(△) | | |
| Mizoue et al.(2006)日本 | 健康族群(177) | 尿液，HPLC | ＋ | | － | | | | | 吸菸與 BMI 交互作用(＋) |
| Kuo et al.(2003)台灣 | 鉻電鍍工廠員工(50)<br>對照組(20) | 尿液，HPLC-ECD | △ | △ | | ＋ | | | 尿鉻(＋) | 感冒(＋) |
| Chuang et al.(2003)台灣 | 計程車司機(95)<br>社區居民(75) | 尿液，ELISA | ＋ | △ | | | △ | | 計程車司機(＋) | 嚼檳榔(＋) |
| Nilsson et al.(2004)瑞典 | 船上引擎室工人(36)<br>非暴露船員(34) | 尿液，HPLC-ECD | △ | △ | | | | | | 尿中 1-OHP(＋) |
| Liu et al.(2005)中國大陸 | 煉焦爐工人(47)<br>非暴露工人(31) | 尿液，HPLC-ECD | △ | △ | － | △ | | | 煉焦爐工人(＋) | |
| Wu et al.(2003)台灣 | 煉焦爐工人(217) | 尿液，ELISA | △ | △ | △ | △ | | 服用綜合維他命(－) | | 嚼檳榔(△) |
| Kristenson et al.(2003)立陶宛 | 立陶宛 50 歲<br>健康男人(109)<br>瑞典 50 歲<br>健康男人(99) | 尿液，HPLC-ECD | ＋ | | △ | | | 血清中 Vit.E(△)<br>血清中胡蘿蔔素(－) | | |

＋ 正相關、－ 負相關、△ 無顯著相關; *P 值＜0.05

表 3 游離二氧化矽基因毒性之研究

| 年份 | 作者 | 對象 | 結果 |
|---|---|---|---|
| 1990 | Pairon et al. | 人類的淋巴細胞與單核白血球 | 鱗矽石的濃度增加會使細胞姊妹染色體交換頻率增加 |
| 1995 | Nagalakshmi et al. | 中國大鼠的肺部纖維母細胞(V79)以及人類的胚胎肺部細胞（Hel 299） | 二氧化矽在老鼠與人類的細胞都有微核的形成 |
| 1996 | Xiaorong et al. | 中國大鼠肺部纖維組織母細胞（V79細胞） | 發現二氧化矽會引起染色體變異 |
| 2003 | Basaran et al. | 陶瓷工廠與鑄造廠員工 | 職業上暴露到二氧化矽的員工有 DNA 損害增加 |

表 4 研究對象基本人口學變項之分佈

| 變 項 | | 總人數 | % | 吸菸 | 非吸菸 | Mean | P 值 |
|---|---|---|---|---|---|---|---|
| 年齡（歲） | | 74 | - | 47.93 ± 10.0 | 47.44 ± 10.6 | 47.64 ± 10.0 | 0.810§ |
| 工作年資(年) | | 74 | - | 18.10 ± 10.4 | 19.82 ± 11.6 | 19.15 ± 11.1 | 0.460§ |
| BMI （$kg/m^2$） | | 74 | - | 25.17 ± 2.9 | 24.78 ± 2.9 | 24.94 ± 2.9 | 0.570§ |
| 累積暴露濃度($mg/m^3$*year) | | 74 | - | 10.50 ± 6.9 | 13.51 ± 9.8 | 12.33 ± 8.9 | 0.280§ |
| 吸菸習慣 | 吸菸 | 29 | 39.2 | - | - | - | - |
| | 不吸菸 | 45 | 60.8 | - | - | - | |
| 教育程度 | 國中以下 | 36 | 48.7 | 18 | 18 | - | 0.141* |
| | (含)國中以上 | 33 | 44.6 | 10 | 23 | - | |
| | Missing values | 5 | 6.7 | 1 | 4 | - | |
| 吃檳榔習慣 | 有 | 19 | 25.6 | 14 | 5 | - | **0.0007*** |
| | 無 | 52 | 70.3 | 14 | 38 | - | |
| | Missing values | 3 | 4.1 | 1 | 2 | - | |
| 攝取 Vitamin C | 有 | 10 | 13.5 | 4 | 6 | - | 1.000* |
| | 無 | 62 | 83.8 | 24 | 38 | - | |
| | Missing values | 2 | 2.7 | 1 | 1 | - | |
| 攝取 Vitamin E | 有 | 5 | 6.7 | 3 | 2 | - | 0.360* |
| | 無 | 66 | 89.2 | 24 | 42 | - | |
| | Missing values | 3 | 4.1 | 2 | 1 | - | |
| 攝取 Multi-vitamins | 有 | 14 | 18.9 | 6 | 8 | - | 0.760* |
| | 無 | 57 | 77 | 21 | 36 | - | |
| | Missing values | 3 | 4.1 | | 1 | - | |

§:Kruskall Wallis test

*:Fisher's exact test

表 5 研究對象基本人口學變項依不同廠別之分佈

| 變 項 | A 廠 19 人 | B 廠 28 人 | C 廠 27 人 | P 值 |
|---|---|---|---|---|
| | mean±SD | mean±SD | mean±SD | |
| 年齡（歲） | 41.42±13.34 | 51.36±6.43 | 48.15±9.4 | **0.01§** |
| BMI （kg/m²） | 24.69±2.89 | 24.92±2.65 | 25.12±3.21 | 0.74§ |
| 工作年資(年) | 11.42±7.75 | 27.64±5.71 | 15.78±11.62 | **<.0001§** |
| | N（%） | N（%） | N（%） | |
| 作業類別 | | | | 0.17* |
| 拆模、噴砂、研磨 | 4 (21%) | 1 (3.6%) | 5 (18%) | |
| 造模、合模、噴模、電爐、燒鑄 | 11 (58%) | 14 (50%) | 15 (56%) | |
| 其他的行政清潔人員 | 4 (21%) | 13 (46.4%) | 7 (26%) | |
| 累積暴露類別 | | | | **<.0001#** |
| 高暴露 | 3 (15%) | 16 (57%) | 1 (4%) | |
| 中暴露 | 10 (53%) | 12 (43%) | 13 (48%) | |
| 低暴露 | 6 (32%) | 0 (0%) | 13 (48%) | |
| 籍貫 | | | | 0.13* |
| 閩南 | 16(84) | 26(93) | 20(74) | |
| 閩南以外 | 2(11) | 2(7) | 7(26) | |
| 教育程度 | | | | **0.047*** |
| 國中以下 | 9(47) | 12(43) | 20(74) | |
| (含)國中以上 | 10(53) | 16(57) | 7(26) | |
| 婚姻狀況 | | | | **0.006*** |
| 單身 | 6(32) | 1(4) | 2(7) | |
| 已婚 | 10(53) | 26(93) | 25(93) | |
| 吸菸習慣 | | | | 0.97# |
| 吸菸 | 7(37) | 11(39) | 11(41) | |
| 不吸菸 | 12(63) | 17(61) | 16(59) | |
| 吃檳榔習慣 | | | | 0.2# |
| 無 | 11(58) | 21(75) | 20(74) | |
| 有 | 8(42) | 5(18) | 6(22) | |
| Vitamin C | | | | 0.12* |
| 無 | 14(74) | 24(86) | 24(89) | |
| 有 | 4(21) | 1(4) | 1(4) | |
| VitaminE | | | | 0.84* |
| 無 | 16(84) | 25(89) | 25(93) | |

| | | | | |
|---|---|---|---|---|
| | 有 | 2(11) | 1(4) | 2(7) | |
| Multi-vitamins | | | | | 0.35* |
| | 無 | 13(68) | 21(75) | 23(85) | |
| | 有 | 5(26) | 6(21) | 3(11) | |
| HBsAg | | | | | 0.43* |
| | 無 | 19(100) | 25(89) | 25(93) | |
| | 有 | 0(0) | 3(11) | 2(7) | |
| GOT | | | | | 0.09* |
| | 正常 | 18(95) | 27(96) | 21(78) | |
| | 異常 | 1(5) | 1(4) | 6(22) | |
| GPT | | | | | 0.69* |
| | 正常 | 17(89) | 25(89) | 22(81) | |
| | 異常 | 2(11) | 3(11) | 5(19) | |
| r-GT | | | | | **0.05*** |
| | 正常 | 16(84) | 27(96) | 20(74) | |
| | 異常 | 3(16) | 1(4) | 7(26) | |
| 塵肺症--N(%) | | | | | **0.04#** |
| | 正常 | 14(74) | 12(43) | 20(74) | |
| | 異常 | 4(21) | 14(50) | 7(26) | |
| | | mean±SD(N) | mean±SD(N) | mean±SD(N) | |
| FEV1 (L) | | | | | |
| | Smoker | 3.58±1(7) | 2.68±0.53(11) | 3.53±0.96(11) | **0.03§** |
| | Non-smoker | 3.2±0.55(12) | 2.69±0.47(17) | 3.21±0.72(16) | **0.03§** |
| | Subtotal | 3.34±0.74(19) | 2.69±0.48(28) | 3.34±0.82(27) | **0.0006§** |
| | *p* value§ | 0.74 | 0.95 | 0.64 | |
| FVC(L) | | | | | |
| | Smoker | 4.17±0.98(7) | 4.05±0.6(11) | 4.03±1.28(11) | 0.68§ |
| | Non-smoker | 3.82±0.75(12) | 3.77±0.71(17) | 3.66±0.78(16) | 0.81§ |
| | Subtotal | 3.95±0.83(19) | 3.88±0.67(28) | 3.81±1.01(27) | 0.57§ |
| | *p* value§ | 0.64 | 0.57 | 0.88 | |
| FEV1 %pred | | | | | |
| | Smoker | 99.2±20.2(7) | 89.7±17.2(11) | 115.2±23.9(11) | **0.02§** |
| | Non-smoker | 94.9±7.85(12) | 92.3±10.7(17) | 106.7±12.2(16) | **0.001§** |
| | Subtotal | 96.5±13.3(19) | 91.3±13.3(28) | 110.1±18(27) | **<.0001§** |
| | *p* value§ | 1 | 0.79 | 0.76 | |
| FVC%pred | | | | | |
| | Smoker | 104.5±19.9(7) | 112.2±17.5(11) | 111.2±30.8(11) | 0.69§ |
| | Non-smoker | 98.7±13.6(12) | 106.1±14.8(17) | 102±15.6(16) | 0.47§ |

| | | | | |
|---|---|---|---|---|
| Subtotal | 100.82±16(19) | 108.5±15.9(28) | 105.7±23(27) | 0.38§ |
| *p* value§ | 0.79 | 0.57 | 0.73 | |
| FEV1/FVC % | | | | |
| Smoker | 85.1±6.27(7) | 66.7±10.5(11) | 85.8±5.1(11) | **0.0002§** |
| Non-smoker | 84.4±5.6(12) | 71.6±7.37(17) | 87.7±6.9(16) | **<.0001§** |
| Subtotal | 84.7±5.7(19) | 69.7±8.9(28) | 86.9±6.2(27) | **<.0001§** |
| *p* value§ | 0.94 | 0.51 | 0.76 | |
| Urine 8-OHdG (ng/ml) | | | | |
| Smoker | 10.13±5.2(5) | 8.37±4(11) | 29.4±55.8(10) | 0.48§ |
| Non-smoker | 20.1±20.5(6) | 8±4.5(17) | 8.13±6.05(16) | 0.89§ |
| Subtotal | 15.6±15.7(11) | 8.14±4.2(28) | 16.94±35.3(26) | 0.55§ |
| *p* value§ | 1 | 0.88 | 0.55 | |
| Urine 8-OHdG/Cr (μg/g) | | | | |
| Smoker | 5.49±4.42(5) | 3.78±1.34(11) | 6.13±4.61(10) | 0.68§ |
| Non-smoker | 7.27±7.1(6) | 4.3±2.2(17) | 4.52±2.45(16) | 0.97§ |
| Subtotal | 6.46±5.82(11) | 4.1±1.9(28) | 5.14±3.45(26) | 0.74§ |
| *p* value§ | 1 | 1 | 0.79 | |
| TAC | | | | |
| Smoker | 64.36±23.6(7) | 61.34±31.9(11) | 77.92±37.7(11) | 0.57§ |
| Non-smoker | 60.96±28.4(12) | 57.6±21(17) | 70.53±37.5(16) | 0.76§ |
| Subtotal | 62.21±26.1(19) | 59.1±25.3(28) | 73.54±37.1(27) | 0.4§ |
| *p* value§ | 0.94 | 0.98 | 0.81 | |

§:Kruskall Wallis test

*:Fisher’s exact test

#:卡方檢定

表 6 研究個案肺功能依不同廠別之檢定

| 不同廠別 | 肺活量 FVC% | | FEV1/FVC 比值 | |
|---|---|---|---|---|
| | 正常 N（%） | 異常 N（%） | 正常 N（%） | 異常 N（%） |
| A 廠(n=19 人) | 17(89.5) | 2(10.5) | 19(100) | 0(0) |
| B 廠(n=28 人) | 28(100) | 0(0) | 14(50) | 14(50) |
| C 廠(n=27 人) | 26(96.3) | 1(3.7) | 27(100) | 0(0) |
| P 值 | 0.18* | | <.0001# | |
| 總人數(74 人) | 71(96) | 3(4) | 60(81) | 14(19) |

肺活量 FVC<80%表為異常、FEV1/FVC<70%表為異常

*:Fisher’s exact test

#:卡方檢定

表 7 研究個案肺功能障礙依不同廠別之檢定

| 不同廠別 | 肺功能障礙 N（%） | | | |
|---|---|---|---|---|
| | FEV1/FVC<70%, FVC≥80%(阻塞) | FEV1/FVC≥70%, FVC<80%(侷限) | FEV1/FVC<70%, FVC<80%(混合) | FEV1/FVC≥70%, FVC≥80%：正常 |
| A 廠 (n=19 人) | 0(0) | 2(11) | 0(0) | 17(89) |
| B 廠 (n=28 人) | 14(50) | 0(0) | 0(0) | 14(50) |
| C 廠 (n=27 人) | 0(0) | 1(4) | 0(0) | 26(96) |
| P 值 | <.0001* | | | |
| 總人數 (74 人) | 14(18.9) | 3(4.1) | 0(0) | 57(77.0) |

表 8.影響尿中 8-OHdG/Cr 濃度因子依不同廠別之描述與檢定

| 分析變項 | A 廠<br>mean±SD(N) | B 廠<br>mean±SD(N) | C 廠<br>mean±SD(N) | P value |
|---|---|---|---|---|
| 8-OHdG/Cr<br>g/g creatinine | 6.46±5.82(11) | 4.1±1.89(28) | 5.14±3.45(26) | 0.74[§] |
| 年齡 (year) | | | | |
| 43 歲以下 | 7.85±5.74 | 3.22±0.95 | 4.52±2.11 | 0.59[§] |
| 43-55 歲 | 9±6.4 | 3.91±2.08 | 4.55±3.98 | 0.39[§] |
| 55 歲以上 | 1.22±0.45 | 4.87±1.39 | 8.44±1.74 | **0.006[§]** |
| P value[§] | 0.18 | 0.17 | **0.04** | |
| BMI(kg/m$^2$) | | | | |
| 24 以下 | 7.68±6.7 | 3.74±1.7 | 6.86±4.41 | 0.37[§] |
| 24-27 | 4.07±5.07 | 4.64±2.26 | 4.09±3.31 | 0.42[§] |
| 27 以上 | 8.72(1 人) | 3.63±1.36 | 4.73±1.95 | 0.15[§] |
| P value[§] | 0.64 | 0.56 | 0.27 | |
| 吸菸習慣 | | | | |
| 吸菸 | 5.49±4.42 | 3.78±1.34 | 6.13±4.6 | 0.68[§] |
| 不吸菸 | 7.27±7.1 | 4.3±2.19 | 4.52±2.45 | 0.97[§] |
| P value[b] | 1 | 1 | 0.51 | |
| 吃檳榔習慣 | | | | |
| 無 | 6.95±6.46 | 4.07±2.05 | 5.89±3.67 | 0.38[§] |
| 有 | 5.88±5.63 | 4.34±1.76 | 2.77±1.46 | 0.42[§] |
| P value[b] | 0.93 | 0.6 | 0.06 | |
| HBsAg | | | | |
| 無 | 6.46±5.82 | 4.15±1.96 | 4.78±2.76 | 0.86[§] |
| 有 | 0 人 | 3.65±1.44 | 9.45±9.06 | 0.77 [b] |
| P value[b] | / | 0.88 | 0.41 | |
| GOT | | | | |
| 正常 | 6.46±5.82 | 4.11±1.93 | 5.23±2.74 | 0.54[§] |
| 異常 | 0 人 | 3.79 (1) | 4.85±5.55 | 0.8 [b] |
| P value[b] | / | 0.9 | 0.32 | |
| GPT | | | | |
| 正常 | 6.23±6.08 | 4.03±1.98 | 5.18±2.67 | 0.42[§] |
| 異常 | 8.72 (1 人) | 4.65±0.75 | 4.96±6.21 | 0.48[§] |
| P value[b] | 0.87 | 0.27 | 0.27 | |
| r-GT | | | | |
| 正常 | 6.83±5.99 | 4.11±1.93 | 5.31±2.77 | 0.46[§] |
| 異常 | 2.73 (1 人) | 3.79 (1 人) | 4.67±5.13 | 0.93[§] |
| P value[b] | 0.87 | 0.9 | 0.22 | |

| | | | | |
|---|---|---|---|---|
| 塵肺症 | | | | |
| 正常 | 5.36±5.27 | 4.03±1.85 | 4.86±3.69 | 0.89[§] |
| 異常 | 9.38±7.37 | 4.32±2.06 | 5.89±2.8 | 0.38[§] |
| P value[b] | 0.36 | 0.66 | 0.3 | |
| FVC% | | | | |
| 正常 | 6.23±6.08 | 4.1±1.89 | 4.95±3.38 | 0.82[§] |
| 異常 | 8.72 (1 人) | 0 人 | 9.94 (1 人) | / |
| P value[b] | 0.87 | / | 0.14 | |
| FEV1.0/ FVC% | | | | |
| 正常 | 6.46±5.82 | 4.08±1.68 | 5.14±3.45 | 0.91[§] |
| 異常 | 0 人 | 4.11±2.15 | 0 人 | / |
| P value[b] | / | 0.87 | / | |

[§]:Kruskall Wallis test

[b] :Wilcoxon rank sums test

表 9 研究對象基本人口學變項於不同暴露組別之分佈

| 變 項 | 高暴露 20 人 | 中暴露 35 人 | 低暴露 19 人 | P 值 |
|---|---|---|---|---|
| | mean±SD | mean±SD | mean±SD | |
| 年齡（歲） | 53.3±9.31 | 46.5±10.1 | 43.74±9.59 | **0.003§** |
| BMI （kg/m$^2$） | 24.22±2.18 | 25.55±3.05 | 24.55±3.13 | 0.23§ |
| 工作年資(年) | 29±6.76 | 20.09±9.59 | 7.05±3.22 | **<.0001§** |
| | N（%） | N（%） | N（%） | |
| 籍貫 | | | | **0.01*** |
| 閩南 | 19（95） | 32（91） | 11（58） | |
| 閩南以外 | 1（5） | 3（9） | 7（37） | |
| 教育程度 | | | | **0.03#** |
| 國中以下 | 6（30） | 23（66） | 12（63） | |
| (含)國中以上 | 14（70） | 12（34） | 7（37） | |
| 婚姻狀況 | | | | 0.06* |
| 單身 | 2（10） | 2（6） | 5（26） | |
| 已婚 | 17（85） | 32（91） | 12（63） | |
| 吸菸習慣 | | | | 0.3# |
| 吸菸 | 5（25） | 16（46） | 8（42） | |
| 不吸菸 | 15（75） | 19（54） | 11（58） | |
| 吃檳榔習慣 | | | | 0.38# |
| 無 | 16（80） | 25（71） | 11（58） | |
| 有 | 4（20） | 8（23） | 7（37） | |
| Vitamin C | | | | 0.61* |
| 無 | 16（80） | 29（83） | 17（89） | |
| 有 | 3（15） | 6（17） | 1（5） | |
| VitaminE | | | | 0.58* |
| 無 | 17（85） | 31（89） | 18（95） | |
| 有 | 2（10） | 3（9） | 0 | |
| Multi-vitamins | | | | 0.34* |
| 無 | 13（65） | 29（83） | 15（79） | |
| 有 | 6（30） | 5（14） | 3（16） | |
| HBsAg | | | | **0.05*** |
| 無 | 17（85） | 35（100） | 17（89） | |
| 有 | 3（15） | 0（0） | 2（11） | |
| GOT | | | | 0.06* |
| 正常 | 19（75） | 33（94） | 14（74） | |

| | | | | |
|---|---|---|---|---|
| | 異常 | 1 (5) | 2 (6) | 5 (26) | |
| GPT | | | | | 0.61* |
| | 正常 | 18 (90) | 31 (89) | 15 (79) | |
| | 異常 | 2 (10) | 4 (11) | 4 (21) | |
| r-GT | | | | | 0.15* |
| | 正常 | 19 (95) | 30 (86) | 14 (74) | |
| | 異常 | 1 (5) | 5 (14) | 5 (26) | |
| 塵肺症--N(%) | | | | | 0.11# |
| | 正常 | 9 (45) | 22 (63) | 15 (79) | |
| | 異常 | 9 (45) | 13 (37) | 3 (16) | |
| | | mean±SD(N) | mean±SD(N) | mean±SD(N) | |
| FEV1 (L) | | | | | |
| | Smoker | 2.46±0.32(5) | 3.21±0.73(16) | 3.7±1.19(8) | **0.05§** |
| | Non-smoker | 2.75±0.68(15) | 3.1±0.64(19) | 3.21±0.46(11) | 0.09§ |
| | Subtotal | 2.68±0.61(20) | 3.15±0.67(35) | 3.42±0.86(19) | **0.005§** |
| | *p* value§ | 0.6 | 0.87 | 0.88 | |
| FVC(L) | | | | | |
| | Smoker | 4.1±0.5(5) | 3.91±0.73(16) | 4.38±1.47(8) | 0.76§ |
| | Non-smoker | 3.75±0.86(15) | 3.81±0.75(19) | 3.61±0.53(11) | 0.88§ |
| | Subtotal | 3.84±0.79(20) | 3.85±0.74(35) | 3.93±1.07(19) | 0.91§ |
| | *p* value§ | 0.65 | 0.9 | 0.68 | |
| FEV1 %pred | | | | | |
| | Smoker | 84.28±14.6(5) | 100.7±17.7(16) | 114.4±30.1(8) | 0.08§ |
| | Non-smoker | 93.4±10.8(15) | 99.5±14.8(19) | 102.1±6.8(11) | 0.09§ |
| | Subtotal | 91.1±12.1(20) | 100.1±16(35) | 107±20.4(19) | **0.01§** |
| | *p* value§ | 0.34 | 0.85 | 0.88 | |
| FVC%pred | | | | | |
| | Smoker | 114.4±15.6(5) | 105.6±17.2(16) | 115.9±36(8) | 0.62§ |
| | Non-smoker | 104.7±16(15) | 104±15.5(19) | 97.6±10.5(11) | 0.47§ |
| | Subtotal | 107±16.4(20) | 104.7±16.1(35) | 105.3±26(19) | 0.54§ |
| | *p* value§ | 0.41 | 0.84 | 0.55 | |
| FEV1/FVC % | | | | | |
| | Smoker | 60.7±10.7(5) | 80.7±9.7(16) | 84.9±5.2(8) | **0.004§** |
| | Non-smoker | 73.8±8.12(15) | 81.4±8.9(19) | 89.1±6.5(11) | **0.0004§** |
| | Subtotal | 70.5±10.3(20) | 81.1±9.2(35) | 87.3±6.2(19) | **<.0001§** |
| | *p* value§ | 0.06 | 1 | 0.32 | |
| Urine 8-OHdG (ng/ml) | | | | | |

| | | | | |
|---|---|---|---|---|
| Smoker | 7.12±5.1(5) | 12±6.23(15) | 37±73.5(6) | 0.21§ |
| Non-smoker | 11.34±9.5(15) | 8.4±9.3(16) | 12.2±11.9(8) | 0.42§ |
| Subtotal | 10.3±8.7(20) | 10.14±8(31) | 22.8±48.1(14) | 0.95§ |
| *p* value§ | 0.46 | 0.17 | 0.99 | |
| Urine 8-OHdG/Cr (μg/g) | | | | |
| Smoker | 3.81±2.18(5) | 5.35±3.1(15) | 5.18±5.58(6) | 0.59§ |
| Non-smoker | 5.56±3.57(15) | 3.9±3.6(16) | 5.41±2.94(8) | 0.15§ |
| Subtotal | 5.12±3.32(20) | 4.6±3.4(31) | 5.31±4.08(14) | 0.64§ |
| *p* value§ | 0.8 | 0.13 | 0.57 | |
| TAC | | | | |
| Smoker | 51.67±21.3(5) | 75.32±35.4(16) | 64.9±30.4(5) | 0.36§ |
| Non-smoker | 56.8±22.3(15) | 62.6±30.9(19) | 72.6±35.7(11) | 0.51§ |
| Subtotal | 55.6±21.6(20) | 68.4±33.2(35) | 69.3±32.9(19) | 0.37§ |
| *p* value§ | 0.8 | 0.65 | 0.97 | |

§:Kruskall Wallis test

*:Fisher’s exact test

#:卡方檢定

**備註：**在此累積暴露濃度居於 0～25%之間為低暴露組、25～75%之間為中暴露組、75～100%之間為高暴露組；低暴露組之累積暴露濃度≦5.38 mg/m$^3$*year，中暴露組之累積暴露濃度介於 5.38~18.54 mg/m$^3$*year 之間，高暴露組之累積暴露濃度≧18.54 mg/m$^3$*year

表 10 研究個案肺功能依累積暴露組別之檢定

| 累積暴露組別 | 肺活量 FVC% | | FEV1/FVC 比值 | |
|---|---|---|---|---|
| | 正常 N（%） | 異常 N（%） | 正常 N（%） | 異常 N（%） |
| 高暴露組(20 人) | 19 (95) | 1 (5) | 11 (55) | 9 (45) |
| 中暴露組(35 人) | 34 (97) | 1 (3) | 30 (85.7) | 5 (14.3) |
| 低暴露組(19 人) | 18 (95) | 1 (5) | 19 (100) | 0 (0) |
| P 值 | 1* | | **0.0008*** | |
| 總人數(74 人) | 71(96) | 3(4) | 60(81) | 14(19) |

肺活量 FVC<80%表為異常、FEV1/FVC<70%表為異常

*:Fisher’s exact test

表 11 研究個案肺功能障礙依累積暴露組別之檢定

| 累積暴露組別 | 肺功能障礙 N（%） | | | |
|---|---|---|---|---|
| | FEV1/FVC<70%, FVC≥80%(阻塞) | FEV1/FVC≥70%, FVC<80%(侷限) | FEV1/FVC<70%, FVC<80%(混合) | FEV1/FVC≥70%, FVC≥80%：正常 |
| 高暴露組(20 人) | 9 (45) | 1 (5) | 0 (0) | 10 (50) |
| 中暴露組(35 人) | 5 (14) | 1 (3) | 0 (0) | 29 (83) |
| 低暴露組(19 人) | 0 (0) | 1 (5) | 0 (0) | 18 (95) |
| P 值 | **0.002*** | | | |
| 總人數 (74 人) | 14(18.9) | 3(4.1) | 0(0) | 57(77.0) |

*:Fisher’s exact test

表 12 尿中 8-OHdG/Cr 濃度因子於不同暴露組別之描述與檢定

| 分析變項 | 高暴露 mean±SD(N) | 中暴露 mean±SD(N) | 低暴露 mean±SD(N) | P value |
|---|---|---|---|---|
| 8-OHdG/Cr g/g creatinine | 5.12±3.32(20) | 4.6±3.4 (31) | 5.31±4.08(14) | 0.64§ |
| 年齡 (year) | | | | |
| 43 歲以下 | 14.32 (1 人) | 3.53±1.47 | 5.49±3.15 | 0.09§ |
| 43-55 歲 | 4.52±2.69 | 4.65±4.14 | 4.92±5.57 | 0.87§ |
| 55 歲以上 | 4.47±2.62 | 5.31±2.71 | 6.39 (1 人) | 0.6§ |
| P value§ | 0.24 | 0.33 | 0.37 | |
| BMI(kg/m$^2$) | | | | |
| 24 以下 | 4.97±4.26 | 5.16±4.53 | 8.07±4.91 | 0.27§ |
| 24-27 | 5.51±3.1 | 3.98±3.36 | 3.09±1.71 | 0.36§ |
| 27 以上 | 4.34±1.08 | 4.85±2.37 | 3.49±1.4 | 0.68§ |
| P value§ | 0.78 | 0.6 | 0.12 | |
| 吸菸習慣 | | | | |
| 吸菸 | 3.81±2.18 | 5.35±3.09 | 5.18±5.58 | 0.59§ |
| 不吸菸 | 5.56±3.57 | 3.9±3.63 | 5.41±2.94 | 0.15§ |
| P value[b] | 0.54 | **0.04** | 0.33 | |
| 吃檳榔習慣 | | | | |
| 無 | 4.63±2.71 | 4.93±3.76 | 7.07±4.58 | 0.24§ |
| 有 | 7.08±5.16 | 3.82±2.64 | 2.54±1.3 | 0.3§ |
| P value[b] | 0.32 | 0.82 | **0.03** | |
| HBsAg | | | | |
| 無 | 5.38±3.51 | 4.6±3.4 | 4.62±2.93 | 0.65§ |
| 有 | 3.65±1.44 | 0 人 | 9.45±9.06 | 0.77[b] |
| P value[b] | 0.6 | / | 0.52 | |
| GOT | | | | |
| 正常 | 5.19±3.39 | 4.74±3.47 | 5.04±2.9 | 0.74§ |
| 異常 | 3.79 (1 人) | 2.55±0.02 | 6±6.79 | 0.5§ |
| P value[b] | 1 | 0.36 | 1 | |
| GPT | | | | |
| 正常 | 5.2±3.49 | 4.59±3.51 | 4.95±2.77 | 0.62 |
| 異常 | 4.36±0.81 | 4.71±2.97 | 6.62±8.17 | 0.95 |
| P value[b] | 0.95 | 0.93 | 1 | |
| r-GT | | | | |
| 正常 | 5.19±3.39 | 4.82±3.58 | 5.15±2.82 | 0.71§ |
| 異常 | 3.79 (1 人) | 3.13±1.06 | 5.72±6.93 | 0.92§ |
| P value[b] | 1 | 0.54 | 0.52 | |
| 塵肺症 | | | | |

| | | | | |
|---|---|---|---|---|
| 正常 | 5.32±3.95 | 3.93±2.78 | 5.41±4.37 | 0.52[§] |
| 異常 | 5.41±3.02 | 5.53±4.04 | 4.72±2.36 | 0.92[§] |
| P value[b] | 0.72 | 0.24 | 0.93 | |
| FVC% | | | | |
| 正常 | 4.87±3.2 | 4.47±3.37 | 5.31±4.08 | 0.6[§] |
| 異常 | 9.94 (1 人) | 8.72 (1 人) | 0 人 | / |
| P value[b] | 0.17 | 0.24 | / | |
| FEV1/ FVC% | | | | |
| 正常 | 5.32±4.06 | 4.96±3.6 | 5.31±4.08 | 0.93[§] |
| 異常 | 4.87±2.32 | 2.75±0.81 | 0 人 | 0.11[b] |
| P value[b] | 0.7 | 0.14 | / | |

[§]: Kruslal Wallis test

[b]:Wilcoxon rank sum test

表 13　個人累積暴露濃度與其健康效應之單變項迴歸分析

| 依變項 | 相關係數 | 檢定之 P 值 | 迴歸係數 | 檢定之 P 值 |
|---|---|---|---|---|
| FEV1 (L) | | | | |
| Smoker | -0.39 | **0.04** | -0.06 | **0.01** |
| Non-smoker | -0.36 | **0.02** | -0.02 | **0.02** |
| Subtotal | -0.37 | **0.001** | -0.03 | **0.0008** |
| FVC(L) | | | | |
| Smoker | 0.01 | 0.94 | -0.01 | 0.6 |
| Non-smoker | 0.04 | 0.78 | -0.003 | 0.8 |
| Subtotal | 0.02 | 0.85 | -0.009 | 0.45 |
| FEV1 %pred | | | | |
| Smoker | -0.36 | **0.05** | -1.45 | **0.02** |
| Non-smoker | -0.32 | **0.03** | -0.36 | **0.05** |
| Subtotal | -0.33 | **0.004** | -0.64 | **0.004** |
| FVC%pred | | | | |
| Smoker | 0.14 | 0.48 | -0.07 | 0.92 |
| Non-smoker | 0.17 | 0.27 | 0.14 | 0.53 |
| Subtotal | 0.14 | 0.22 | 0.02 | 0.92 |
| FEV1/FVC % | | | | |
| Smoker | -0.63 | **0.0003** | -1.21 | **<.0001** |
| Non-smoker | -0.63 | **<.0001** | -0.56 | **<.0001** |
| Subtotal | -0.63 | **<.0001** | -0.67 | **<.0001** |
| Urine 8-OHdG (ng/ml) | | | | |
| Smoker | -0.11 | 0.59 | -1.41 | 0.17 |
| Non-smoker | -0.06 | 0.71 | -0.09 | 0.58 |
| Subtotal | -0.1 | 0.42 | -0.46 | 0.16 |
| Urine 8-OHdG/Cr (μg/g) | | | | |
| Smoker | -0.1 | 0.64 | -0.12 | 0.24 |
| Non-smoker | -0.07 | 0.69 | -0.02 | 0.79 |
| Subtotal | -0.08 | 0.53 | -0.04 | 0.4 |
| TAC | | | | |
| Smoker | -0.04 | 0.82 | -0.39 | 0.66 |
| Non-smoker | -0.15 | 0.32 | -0.43 | 0.35 |
| Subtotal | -0.12 | 0.3 | -0.46 | 0.26 |

表 14 研究個案其抗氧化能力依攝食頻率之趨勢檢定

| 抗氧化能力(TAC) | 個案數 | Mean ± SD | (≤1 次/週) | | (>1 次/週 ~1/天) | | (≥2 次/天) | | *p*-value(Krus kal- Wallis test) | *p*-value (趨勢檢定) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | No. | Mean ± SD | No. | Mean ± SD | No. | Mean ± SD | | |
| 深海魚 | 72 | 65.58 ± 30.9 | 34 | 69.37 ± 32 | 28 | 57.88 ± 28.6 | 10 | 74.25 ± 31.7 | 0.14 | 0.91 |
| 淡水魚 | 73 | 65.31 ± 30.8 | 24 | 64.14 ± 32.8 | 36 | 64.3 ± 30.8 | 13 | 70.3 ± 28.6 | 0.71 | 0.58 |
| 淡色蔬菜 | 73 | 65.15 ± 30.8 | 8 | 69.97 ± 24.6 | 52 | 67.37 ± 33.6 | 13 | 53.34 ± 19.1 | 0.36 | 0.18 |
| 深綠色蔬菜 | 73 | 65.69 ± 30.5 | 12 | 59.41 ± 30.7 | 50 | 70.71 ± 31.5 | 11 | 49.69 ± 18.5 | 0.11 | 0.68 |
| 胡蘿蔔 | 74 | 65.15 ± 30.6 | 35 | 66.14 ± 27.9 | 34 | 64.67 ± 33 | 5 | 61.58 ± 38.6 | 0.79 | 0.75 |
| 番茄 | 74 | 65.15 ± 30.6 | 47 | 63.55 ± 30.1 | 25 | 65.24 ± 31 | 2 | 101.79 ± 28.5 | 0.22 | 0.3 |
| 柑橘類水果 | 73 | 64.85 ± 30.7 | 29 | 68.56 ± 29.5 | 32 | 65.51 ± 33.5 | 12 | 54.11 ± 25.2 | 0.34 | 0.18 |
| 柿子、木瓜、芒果 | 74 | 65.15 ± 30.6 | 36 | 69.05 ± 31.3 | 30 | 61.76 ± 30.7 | 8 | 60.37 ± 28.4 | 0.54 | 0.32 |
| 當季水果 | 74 | 65.15 ± 30.6 | 22 | 64.9 ± 30.9 | 38 | 66.49 ± 31.2 | 14 | 61.94 ± 30.6 | 0.83 | 0.83 |

表 15　研究個案其健康效應依吸菸與否之描述及檢定

| 健康效應 | mean±SD | N | Smoker | Nonsmoker | P value[b] |
|---|---|---|---|---|---|
| | | | mean±SD(N) | mean±SD(N) | |
| FEV1(L) | 3.09±0.8 | 74 | 3.22±0.9 (29) | 3.01±0.6 (45) | 0.58 |
| FVC(L) | 3.87±0.8 | 74 | 4.07±1 (29) | 3.74±0.7 (45) | 0.18 |
| FEV1%pred | 99.49±17.2 | 74 | 101.66±22.9(29) | 98.1±12.2 (45) | 0.65 |
| FVC %pred | 105.5±18.8 | 74 | 109.95±23.3(29) | 102.65±14.7 (45) | 0.18 |
| FEV1/FVC% | 79.82±10.7 | 74 | 78.39±12 (29) | 80.75±9.9 (45) | 0.61 |
| 8-OHdG | 12.9±23.5 | 65 | 16.8±35.2 (26) | 10.32±9.8 (39) | 0.33 |
| 8-OHdG/crea | 4.9±3.5 | 65 | 5.02±3.6 (26) | 4.85±3.5 (39) | 0.74 |
| TAC | 65.16±30.6 | 74 | 68.36±32.4 (29) | 63.09±25.6 (45) | 0.57 |

b: Wilcoxon rank sums test

8-OHdG, 8-OHdG/crea excludes 9 extreme cases

表 16　研究個案其健康效應依 BMI 分組之趨勢檢定

| 健康效應 | 個案數 | Mean ± SD | BMI < 24 | | 27> BMI≥24 | | BMI ≥27 | | *p*-value (Kruskal-Wallis test) | *p*-value（趨勢檢定） |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | No. | Mean ± SD | No. | Mean ± SD | No. | Mean ± SD | | |
| 累積暴露濃度 | 74 | 12.33 ± 8.9 | 27 | 11.69 ± 8.9 | 27 | 14.28 ± 9.9 | 20 | 10.55 ± 7.0 | 0.760 | 0.760 |
| FEV1(L) | 74 | 3.09 ± 0.8 | 27 | 3.32 ± 0.8 | 27 | 3.08 ± 0.8 | 20 | 2.8 ± 0.5 | 0.100 | **0.018** |
| FVC(L) | 74 | 3.87 ± 0.8 | 27 | 4.14 ± 1.0 | 27 | 3.82 ± 0.8 | 20 | 3.6 ± 0.6 | 0.090 | **0.018** |
| FEV1%pred | 74 | 99.49 ± 17.2 | 27 | 103.36 ± 18.7 | 27 | 99.72 ± 18 | 20 | 94.0 ± 12.5 | 0.250 | 0.065 |
| FVC%pred | 74 | 105.5 ± 18.8 | 27 | 111.04 ± 22.9 | 27 | 104.33 ± 15.5 | 20 | 99.65 ± 15 | 0.150 | **0.036** |
| FEV1/FVC% | 74 | 79.82 ± 10.7 | 27 | 80.6 ± 10.3 | 27 | 80.29 ± 9.3 | 20 | 78.14 ± 13.2 | 0.930 | 0.962 |
| 8-OHdG/crea | 65 | 4.9 ±3.5 | 23 | 5.85 ±4.53 | 26 | 4.34 ±3.06 | 16 | 4.5 ± 2 | 0.62 | 0.19 |
| TAC | 74 | 65.16 ± 30.6 | 27 | 54.31 ± 20.3 | 27 | 68.48 ± 32.1 | 20 | 75.31 ± 36.5 | 0.140 | **0.016** |

表 17 研究個案其健康效應依暴露組別之趨勢檢定

| 健康效應 | 個案數 | Mean ± SD | 累積暴露組別 低暴露組 | | 中暴露組 | | 高暴露組 | | *p*-value (Kruskal-Wallis test) | *p*-value (Trend test) |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | No. | Mean ± SD | No. | Mean ± SD | No. | Mean ± SD | | |
| FEV1(L) | 74 | 3.09 ± 0.8 | 19 | 3.42 ± 0.9 | 35 | 3.15 ± 0.7 | 20 | 2.68 ± 0.6 | **0.005** | **0.002** |
| FVC(L) | 74 | 3.87 ± 0.8 | 19 | 3.93 ± 1.1 | 35 | 3.85 ± 0.7 | 20 | 3.84 ± 0.8 | 0.91 | 0.72 |
| FEV1%pred | 74 | 99.49 ± 17.2 | 19 | 107.23 ± 20.4 | 35 | 100.08 ± 16 | 20 | 91.11 ± 12.1 | **0.01** | **0.003** |
| FVC%pred | 74 | 105.5 ± 18.8 | 19 | 105.31 ± 25.6 | 35 | 104.69 ± 16.1 | 20 | 107.1 ± 16.4 | 0.54 | 0.76 |
| FEV1/FVC% | 74 | 79.82 ± 10.7 | 19 | 115.7 ± 7.2 | 35 | 108.86 ± 12.8 | 20 | 98.22 ± 15.1 | **0.0002** | **<.0001** |
| 8-OHdG/crea | 65 | 4.9 ± 3.5 | 14 | 5.31 ± 4.08 | 31 | 4.6 ± 3.4 | 20 | 5.12 ± 3.32 | 0.64 | 0.94 |
| TAC | 74 | 65.16 ± 30.6 | 19 | 69.31 ± 32.9 | 35 | 68.39 ± 33.2 | 20 | 55.55 ± 21.6 | 0.37 | 0.16 |
| BMI | 74 | 24.9±42.9 | 19 | 24.55±3.13 | 35 | 25.55±3.05 | 20 | 24.22±2.18 | 0.23 | |

表 18　勞工健康效應與各影響因子間之單變項迴歸分析

| 自變項 | | 依變項 | | | | |
|---|---|---|---|---|---|---|
| | | FEV1%pred | FVC%pred | FEV1/FVC% | 8-OHdG/crea | TAC |
| 累積暴露濃度 | coefficient | -0.64 | 0.02 | -0.67 | -0.04 | -0.46 |
| | P value | **0.004** | 0.92 | **<0.0001** | 0.4 | 0.26 |
| Vit C | coefficient | 4.57 | 5.88 | 0.44 | 1.87 | -10.64 |
| | P value | 0.42 | 0.35 | 0.93 | 0.14 | 0.32 |
| Vit E | coefficient | 11.15 | 12.81 | 1.59 | 1.56 | 3.27 |
| | P value | 0.14 | 0.14 | 0.8 | 0.34 | 0.82 |
| Vit multi | coefficient | 11.54 | 13.28 | 1.77 | 1.54 | -2.86 |
| | P value | **0.02** | **0.02** | 0.67 | 0.16 | 0.76 |
| BMI | coefficient | -1.7 | -2.18 | -0.26 | -0.23 | 3.36 |
| | P value | **0.01** | **0.004** | 0.55 | 0.15 | **0.006** |
| 8-OHdG/crea | coefficient | 0.73 | 0.45 | 0.55 | -- | -0.8 |
| | P value | 0.26 | 0.52 | 0.28 | -- | 0.45 |

表 19　研究個案其肺功能與各影響因子之複迴歸分析

| 健康效應 | Age | BMI | Smoke | 累積暴露濃度 | TAC | Vitamin Intake | Adj-$R^2$ |
|---|---|---|---|---|---|---|---|
| FEV1(L) | –0.02 | –0.08 | 0.16 | –0.02 | 0.005 | 0.38 | 0.37 |
| *p*-value | **0.003** | **0.003** | 0.26 | **0.04** | 0.06 | **0.05** | |
| FVC(L) | –0.03 | –0.09 | 0.38 | 0.007 | 0.003 | 0.31 | 0.21 |
| *p*-value | **0.01** | **0.006** | **0.04** | 0.55 | 0.40 | 0.20 | |
| FEV1%pred | 0.34 | –2.48 | 1.09 | –0.77 | 0.15 | 8.80 | 0.26 |
| *p*-value | 0.09 | **0.0003** | 0.76 | **0.0009** | **0.01** | 0.07 | |
| FVC%pred | –0.13 | –2.34 | 8.27 | 0.16 | 0.07 | 5.73 | 0.11 |
| *p*-value | 0.57 | **0.004** | 0.06 | 0.56 | 0.32 | 0.31 | |
| FEV1/FVC% | –0.07 | –0.44 | –4.57 | –0.66 | 0.07 | 3.65 | 0.36 |
| *p*-value | 0.53 | 0.25 | **0.03** | **<0.0001** | 0.06 | 0.19 | |

表 20　A 廠介入改善前後勞工之基本人口學變項

| 變項 | No. | % |
|---|---|---|
| 年齡[a] | 44.3±11.2 | |
| BMI (kg/m$^2$)[a] | 25.17±3.09 | |
| 工作年資[a] | 13.3±18.3 | |
| 教育程度 | | |
| 高中以下 | 13 | 59.1 |
| (含)高中以上 | 7 | 31.8 |
| Missing value | 2 | 9.1 |
| 作業類別 | | |
| 合模 | 9 | 40.9 |
| 噴模 | 2 | 9.1 |
| 造模 | 10 | 45.5 |
| 合模&造模 | 1 | 4.5 |
| 吸菸習慣 | | |
| 吸菸 | 12 | 54.5 |
| 不吸菸 | 10 | 45.5 |
| 胸部 X-光判讀 | | |
| ILO (0/0) | 15 | 68.2 |
| ILO (1/0) | 5 | 22.7 |
| ILO (1/1) | 2 | 9.1 |
| 肺功能障礙 | | |
| 正常 (FEV1/FVC≥70%, FVC≥80%) | 17 | 77.3 |
| 阻塞型肺功能障礙 (FEV1/FVC<70%, FVC≥80%) | 3 | 13.6 |
| 侷限型肺功能障礙 (FEV1/FVC≥70%, FVC<80%) | 2 | 9.1 |

Abbreviations: BMI, Body Mass Index; ILO, International Labor Organization
[a]Mean±SD

表 21　針對 A 廠介入改善前後之環測及勞工健康效應追蹤

| Exposure and Effects | 改善前 | 改善後 | *P value*[a] |
|---|---|---|---|
| 環測暴露 | mean±SD | mean±SD | |
| 可呼吸性粉塵濃度 ($mg/m^3$) | 2.87±1.38 | 1.60±0.70 | 0.07 |
| 可呼吸性 $SiO_2$ 濃度($mg/m^3$) | 0.43±0.25 | 0.18±0.11 | **<0.05** |
| 健康效應 | | | |
| FEV1 (L) | | | |
| Smoker | 2.87±0.98 | 3.59±1.01 | 0.12 |
| Non-smoker | 3.18±0.55 | 4.09±0.52 | **<0.05** |
| Subtotal | 3.02±0.74 | 3.87±0.86 | **<0.05** |
| *p* value[§] | 0.25 | 0.18 | |
| FVC(L) | | | |
| Smoker | 3.57±0.90 | 4.45±0.96 | 0.059 |
| Non-smoker | 3.77±0.70 | 4.90±0.62 | **<0.05** |
| Subtotal | 3.71±0.76 | 4.73±0.94 | **<0.05** |
| *p* value[§] | 0.424 | 0.183 | |
| FEV1 %pred | | | |
| Smoker | 89.6±22.61 | 111.98±24.86 | **<0.05** |
| Non-smoker | 93.81±8.13 | 123.01±15.31 | **<0.05** |
| Subtotal | 90.95±15.66 | 117.36±20.86 | **<0.05** |
| *p* value[§] | 0.53 | 0.60 | |
| FVC%pred | | | |
| Smoker | 95.54±19.08 | 118.43±21.68 | **<0.05** |
| Non-smoker | 97.36±12.43 | 127.47±11.37 | **<0.05** |
| Subtotal | 96.97±14.50 | 123.67±18.81 | **<0.05** |
| *p* value[§] | 0.53 | 0.29 | |
| FEV1/FVC % | | | |
| Smoker | 79.12±10.00 | 80.16±6.92 | 0.92 |
| Non-smoker | 84.64±5.60 | 83.70±3.67 | 0.82 |
| Subtotal | 81.12±8.48 | 81.71±6.28 | 0.98 |
| *p* value[§] | 0.37 | 0.21 | |
| Urine 8-OHdG (ng/ml) | | | |
| Smoker | 8.77±4.89 | 16.39±9.21 | 0.07 |
| Non-smoker | 15.54±15.64 | 11.94±9.47 | 0.46 |
| Subtotal | 12.15±13.83 | 14.17±9.40 | 0.53 |
| *p* value[§] | 0.62 | 0.31 | |
| Urine 8-OHdG/Cr (μg/g) | | | |
| Smoker | 4.27±3.35 | 9.33±4.23 | **<0.05** |
| Non-smoker | 6.03±5.29 | 7.78±5.61 | 0.48 |
| Subtotal | 5.15±4.41 | 8.55±4.91 | **<0.05** |
| *p* value[§] | 0.49 | 0.41 | |

[a]：Comparison between the baseline and follow-up periods (Wilcoxon sign rank test)
[§]：Comparison between smokers and non-smokers (Kruskall-Wallis test)

表 22　針對 A 廠介入改善前後健康效應之 GEE 檢定

| Variables | log Urinary 8-OHdG | | log Urinary 8-OHdG/Cr | | log FEV1(L) | | log FVC (L) | | logFEV1%pred | | logFVC%pred | | logFEV1/FVC% | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *β* | *p*-value | *β* | *p*-value | *β* | *p*-value | *β* | *p*-value | *β* | *p*-value | *β* | *p*-value | *β* | *p*-value |
| Age (year) | 0.001 | 0.94 | 0.004 | 0.61 | -0.005 | **0.04** | -0.006 | **<0.001** | 0.001 | 0.69 | -0.003 | 0.06 | 0.001 | 0.13 |
| BMI (kg/m$^2$) | -0.011 | 0.70 | -0.013 | 0.47 | -0.006 | 0.25 | -0.005 | 0.28 | -0.003 | 0.53 | -0.003 | 0.48 | 0.001 | 0.85 |
| Smoker (Yes/ no) | 0.034 | 0.83 | -0.012 | 0.91 | -0.011 | 0.74 | 0.022 | 0.42 | -0.036 | 0.21 | 0.007 | 0.76 | -0.033 | **0.01** |
| Cumulative exposure (mg/m$^3$*year) | -0.001 | 0.93 | -0.006 | 0.42 | 0.001 | 0.70 | 0.001 | 0.48 | 0.001 | 1.00 | 0.001 | 0.69 | 0.001 | 0.92 |
| ILO grade ( 1/0 above vs 0/0) | -0.356 | 0.16 | -0.271 | 0.11 | 0.010 | 0.84 | 0.057 | 0.18 | -0.008 | 0.86 | 0.046 | 0.21 | -0.048 | **0.02** |
| Time (follow-up vs baseline) | 0.108 | 0.50 | 0.277 | 0.08 | 0.103 | **<0.001** | 0.106 | **<0.001** | 0.104 | **<0.001** | 0.106 | **<0.001** | -0.002 | 0.65 |
| Intercept | 1.314 | 0.10 | 0.931 | 0.08 | 0.834 | **<0.001** | 0.901 | **<0.001** | 2.024 | **<0.001** | 2.158 | **<0.001** | 1.889 | **<0.001** |

Abbreviation: ILO, International Labour Organization

表 23　B 廠勞工 DNA 傷害與基本人口學變項及習慣之關係

| 變項 | 頭尾比例(L/H) | | | 尾部長度(TL) | | 尾部動量(TEM) | | Oliver 尾矩(OTM) | |
|---|---|---|---|---|---|---|---|---|---|
| | N | Mean±SD | p-value[b] | Mean±SD | p-value[b] | Mean±SD | p-value[b] | Mean±SD | p-value[b] |
| 所有勞工 | 27 | 7.75±1.28 | | 287.43±61.23 | | 184.75±59.19 | | 75.7±31.1 | |
| 年齡(歲) | | | 0.85 | | 0.33 | | 0.33 | | 0.26 |
| ＜50 歲 | 7 | 7.54±0.71 | | 306.56±45.43 | | 201.78±46.44 | | 85.82±25.15 | |
| ≧50 歲 | 20 | 7.58±1.44 | | 280.74±65.55 | | 178.79±63 | | 72.16±32.76 | |
| BMI(kg/m$^2$) | | | 0.94 | | 0.86 | | 0.98 | | 0.82 |
| ＜24 | 9 | 7.52±1.38 | | 285.34±68.35 | | 186.51±64.66 | | 77.33±33.71 | |
| ≧24 | 28 | 7.59±1.26 | | 288.47±59.44 | | 183.87±58.21 | | 74.89±30.71 | |
| 籍貫 | | | 0.33 | | 0.29 | | 0.43 | | 0.75 |
| 閩南 | 25 | 7.48±1.23 | | 284.06±61.68 | | 182.91±61.1 | | 75.17±32.11 | |
| 閩南以外 | 2 | 8.7±1.84 | | 329.6±48.51 | | 207.78±18.2 | | 82.43±17.55 | |
| 教育程度 | | | 0.34 | | 0.64 | | 0.42 | | 0.34 |
| 國中以下 | 11 | 7.8±1.12 | | 297.08±50.95 | | 197.22±52.89 | | 82.24±28.45 | |
| 國中以上 | 16 | 7.41±1.39 | | 280.79±68.22 | | 176.18±63.37 | | 71.22±32.94 | |
| 婚姻狀況 | | | 0.42 | | 0.59 | | 1 | | 0.79 |
| 單身 | 1 | 8.55 | | 332.7 | | 188.91 | | 68.83 | |
| 已婚 | 25 | 7.63±1.21 | | 290.46±57.93 | | 188.93±57.32 | | 77.95±30.66 | |
| 吸菸 | | | 0.18 | | 0.53 | | 0.78 | | 0.82 |
| 有 | 10 | 7.97±0.83 | | 298.9±49 | | 190.05±48.18 | | 76.53±28.37 | |
| 沒有 | 17 | 7.34±1.45 | | 280.68±67.91 | | 181.63±66 | | 75.22±33.45 | |
| 嚼檳榔 | | | 0.48 | | 0.92 | | 0.61 | | 0.56 |
| 有 | 5 | 8.01±0.98 | | 285.34±64.8 | | 176.5±66.08 | | 68.68±38.74 | |
| 沒有 | 20 | 7.55±1.33 | | 290.25±62.23 | | 190.13±59.44 | | 98.73±30.81 | |
| 喝酒 | | | 0.75 | | 0.61 | | 0.9 | | 0.98 |
| 有 | 12 | 7.47±1.27 | | 283.38±72.3 | | 187.44±70.37 | | 77.93±36.91 | |
| 沒有 | 15 | 7.65±1.32 | | 290.67±53.21 | | 182.6±51.04 | | 73.93±26.81 | |
| 運動習慣 | | | 0.14 | | 0.28 | | 0.23 | | 0.28 |
| 有 | 20 | 7.36±1.28 | | 278.24±63.46 | | 175.26±59.71 | | 71.34±30.58 | |
| 沒有 | 7 | 8.17±1.15 | | 313.69±49.1 | | 211.88±52.27 | | 88.18±31.42 | |
| 防護具攜帶情形 | | | 0.18 | | 0.55 | | 0.89 | | 0.96 |
| 有 | 25 | 7.65±1.29 | | 289.4±63.29 | | 185.19±61.48 | | 75.76±32.31 | |
| 沒有 | 2 | 6.55±0.02 | | 262.75±4.88 | | 179.32±17.3 | | 75±10.17 | |

b :wilcoxon rank sum test

表 24　B 廠研究對象暴露量與 DNA 傷害情形描述分析

| 依變項 | 累積暴露量(自變項) | | | |
|---|---|---|---|---|
| | β(SE) | p-value | 相關係數 | p-value |
| L/H | 0.04(0.04) | 0.37 | 0.18 | 0.37 |
| Tail Extent Moment | 2.41(1.88) | 0.21 | 0.25 | 0.21 |
| Olive Tail Moment | 1.12(0.99) | 0.27 | 0.22 | 0.27 |
| Tail Length(μm) | 2.07(1.96) | 0.3 | 0.21 | 0.3 |

表 25　B 廠勞工 DNA 傷害程度之複迴歸分析

| | 未標準化係數 B | 標準誤 S.E | 標準化係數 Beta | T-值 | p-value |
|---|---|---|---|---|---|
| **頭尾比例(L/H)** | | | | | |
| 常數項 | 7.62 | 2.13 | 0 | 3.58 | **0.002** |
| 年齡 | -0.02 | 0.04 | -0.12 | -0.54 | 0.59 |
| 服用維他命 E | -0.09 | 0.79 | -0.02 | -0.12 | 0.91 |
| 吸菸習慣 | -1.22 | 0.54 | -0.47 | -2.25 | **0.04** |
| 籍貫 | 1.77 | 0.92 | 0.37 | 1.93 | 0.07 |
| 教育程度 | -0.71 | 0.59 | -0.28 | -1.2 | 0.24 |
| 累積暴露量 | 0.12 | 0.06 | 0.59 | 2.26 | **0.04** |
| **尾部長度(TL)** | | | | | |
| 常數項 | 363.49 | 101.28 | 0 | 3.59 | **0.002** |
| 年齡 | -3.82 | 2.02 | -0.4 | -1.89 | 0.07 |
| 服用維他命 E | 25.98 | 37.45 | 0.14 | 0.69 | 0.5 |
| 吸菸習慣 | -41.38 | 25.83 | -0.33 | -1.6 | 0.12 |
| 籍貫 | 80.34 | 43.62 | 0.35 | 1.84 | 0.08 |
| 教育程度 | -49.23 | 28.21 | -0.4 | -1.74 | 0.1 |
| 累積暴露量 | 7.65 | 2.62 | 0.76 | 2.92 | **0.009** |
| **尾部動量(ETM)** | | | | | |
| 常數項 | 298.68 | 93.64 | 0 | 3.19 | **0.005** |
| 年齡 | -3.67 | 1.92 | -0.4 | -1.91 | 0.07 |
| 服用維他命 E | 46.57 | 35.62 | 0.25 | 1.31 | 0.21 |
| 吸菸習慣 | -27.07 | 24.57 | -0.23 | -1.1 | 0.28 |
| 籍貫 | 54.11 | 41.49 | 0.24 | 1.3 | 0.2 |
| 教育程度 | -66.33 | 26.84 | -0.56 | -2.47 | **0.02** |
| 累積暴露量 | 8.17 | 2.49 | 0.84 | 3.28 | **0.004** |
| **Oliver 尾矩 (OTM)** | | | | | |
| 常數項 | 142.51 | 51.14 | 0 | 2.79 | **0.01** |
| 年齡 | -1.96 | 1.05 | -0.41 | -1.87 | 0.08 |
| 服用維他命 E | 26.45 | 19.46 | 0.27 | 1.36 | 0.19 |
| 吸菸習慣 | -8.16 | 13.42 | -0.13 | -0.61 | 0.55 |
| 籍貫 | 20.49 | 22.66 | 0.18 | 0.9 | 0.38 |
| 教育程度 | -35.01 | 14.66 | -0.56 | -2.39 | **0.03** |
| 累積暴露量 | 3.95 | 1.36 | 0.78 | 2.9 | **0.009** |

以上迴歸分析註解：有服用維他命 E 比未服用維他命 E;未吸菸比吸菸;閩南以外比閩南;國中以上程度比未滿國中程度

表 26　B 廠勞工六種細胞激素濃度與相關變項之描述與分析

| 變　　項 | N | IL-2 Mean±SD | IL-4 Mean±SD | IL-6 Mean±SD | IL-10 Mean±S.D | TNF Mean±SD | IFN-γ Mean±SD |
|---|---|---|---|---|---|---|---|
| 所有勞工 | 27 | 10.7±27.3 | 1.72±1.04 | 2.36±1.84 | 1.96±0.99 | 1.47±0.98 | 6.04±7 |
| 年齡(歲) | | | | | | | |
| ＜50 歲 | 7 | 21.57±49.24 | 2.39±0.33 | 2.64±1.66 | 2.16±0.68 | 1.66±0.75 | 8.5±13.28 |
| ≧50 歲 | 20 | 6.9±14.04 | 1.48±1.1 | 2.26±1.93 | 1.89±1.08 | 1.41±1.06 | 5.18±2.88 |
| p-value[b] | | 0.91 | **0.02** | 0.28 | 0.28 | 0.16 | 0.52 |
| BMI(kg/m$^2$) | | | | | | | |
| ＜24 | 9 | 3.82±2.5 | 1.65±1.05 | 1.85±1.09 | 1.88±1.12 | 1.18±1.3 | 8.9±11.29 |
| ≧24 | 18 | 14.14±33.19 | 1.75±1.06 | 2.62±2.1 | 2±0.95 | 1.62±0.78 | 4.62±2.9 |
| p-value[b] | | 0.98 | 0.9 | 0.44 | 1 | 0.31 | 0.23 |
| 籍貫 | | | | | | | |
| 閩南 | 25 | 11±28.42 | 1.85±0.95 | 2.44±1.89 | 2±1.01 | 1.47±1.02 | 6±7.21 |
| 閩南以外 | 2 | 6.98±1.35 | 0 | 1.38±0.22 | 1.42±0.54 | 1.5±0.05 | 6.77±5 |
| p-value[b] | | 0.12 | 0.06 | 0.29 | 0.4 | 1 | 0.55 |
| 教育程度 | | | | | | | |
| 國中以下 | 11 | 8.38±19 | 1.32±1.1 | 1.86±1.64 | 2.16±1.41 | 1.39±1.35 | 3.74±2.52 |
| 國中以上 | 16 | 12.3±32.35 | 1.99±0.93 | 2.7±1.94 | 1.83±0.57 | 1.53±0.67 | 7.63±8.61 |
| p-value[b] | | 0.37 | 0.17 | 0.15 | 0.88 | 0.46 | 0.09 |
| 婚姻狀況 | | | | | | | |
| 單身 | 1 | 10.01 | 2.37 | 8.35 | 1.74 | 2.38 | 8 |
| 已婚 | 25 | 11.16±28.35 | 1.68±1.07 | 2.17±1.43 | 2±1.01 | 1.43±1 | 5.93±7.27 |
| p-value[b] | | 0.18 | 0.59 | 0.11 | 1 | 0.18 | 0.35 |
| 吸菸習慣 | | | | | | | |
| 有 | 10 | 4.02±3.45 | 2.11±0.93 | 2.96±2.36 | 2.14±0.83 | 1.72±1.1 | 5.32±2.81 |
| 沒有 | 17 | 14.63±34.1 | 1.48±1.05 | 2±1.4 | 1.86±1.08 | 1.33±0.91 | 6.47±8.64 |
| p-value[b] | | 0.9 | 0.14 | 0.27 | 0.3 | 0.2 | 0.63 |
| 嚼檳榔 | | | | | | | |
| 有 | 5 | 3.79±2.9 | 2.13±1.31 | 2.83±1.49 | 1.94±0.49 | 1.81±0.3 | 6.45±2.46 |
| 沒有 | 20 | 10.24±29.06 | 1.59±1.02 | 2.041.83 | 1.83±0.88 | 1.26±1 | 6.21±8.06 |
| p-value[b] | | 0.92 | 0.27 | 0.17 | 0.54 | 0.2 | 0.29 |
| 喝酒 | | | | | | | |
| 有 | 12 | 2.93±2.63 | 1.51±1.22 | 1.98±1.39 | 1.72±1.04 | 1.51±0.96 | 4.79±2.39 |
| 沒有 | 15 | 16.91±35.89 | 1.88±0.87 | 2.67±2.13 | 2.15±0.94 | 1.44±1.03 | 11.04±9.17 |
| p-value[b] | | 0.15 | 0.48 | 0.27 | 0.1 | 0.75 | 0.98 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 運動習慣 | | | | | | |
| 有 20 | 6.52±14.09 | 1.73±1.02 | 2.14±1.5 | 1.91±0.88 | 1.44±0.88 | 6.6±7.94 |
| 沒有 7 | 22.64±48.8 | 1.66±1.17 | 3±2.62 | 2.1±1.34 | 1.56±1.32 | 4.47±2.93 |
| p-value[b] | 0.56 | 0.91 | 0.31 | 0.68 | 0.87 | 0.52 |
| 防護具攜帶情形 | | | | | | |
| 有 25 | 6±12.67 | 1.67±1.05 | 2.45±1.85 | 1.92±1 | 1.53±0.98 | 6.43±7.13 |
| 沒有 2 | 69.4±90.07 | 2.35±0.6 | 1.29±1.82 | 2.51±0.98 | 0.79±1.11 | 1.21±1.7 |
| p-value[b] | 0.09 | 0.38 | 0.49 | 0.18 | 0.46 | 0.06 |
| 有胸部方面手術 | | | | | | |
| 有 2 | 5.89±2.88 | 0.7±0.99 | 1.58±0.06 | 1.53±0.38 | 1.47±0.08 | 7.2±4.37 |
| 沒有 23 | 11.8±29.53 | 1.87±0.98 | 2.56±1.9 | 2.02±1.06 | 1.55±1.02 | 6.35±7.39 |
| p-value[b] | 0.39 | 0.12 | 0.51 | 0.55 | 0.72 | 0.39 |
| 心臟病 | | | | | | |
| 有 2 | 6.47±2.07 | 1.03±1.45 | 2.45±1.3 | 1.71±0.13 | 1.74±0.29 | 8.24±2.9 |
| 沒有 21 | 12.17±30.98 | 1.83±1 | 2.62±1.94 | 2.06±1.1 | 1.59±1 | 6.42±7.75 |
| p-value[b] | 0.25 | 0.38 | 0.96 | 1 | 0.87 | 0.25 |
| 高血壓 | | | | | | |
| 有 9 | 3.08±2.81 | 1.62±0.97 | 2.18±1.57 | 1.68±0.31 | 1.43±0.59 | 5.82±3.03 |
| 沒有 15 | 7.95±16.14 | 1.75±1.04 | 2.57±2.16 | 2.12±1.23 | 1.45±1.25 | 6.82±9.1 |
| p-value[b] | 0.47 | 0.81 | 0.74 | 0.77 | 0.86 | 0.51 |

[b]：Wilcoxon rank sum test

表 27　B 廠勞工累積暴露量與六種細胞激素之線性描述與檢定

| 依變項 | 累積暴露量（自變項） | | | |
|---|---|---|---|---|
| | 迴歸係數 | p-value | 相關係數 | p-value |
| IL-2 | -0.02 | 0.98 | 0.09 | 0.65 |
| IL-4 | -0.007 | 0.84 | -0.04 | 0.83 |
| IL-6 | 0.06 | 0.32 | 0.22 | 0.28 |
| IL-10 | -0.03 | 0.3 | -0.32 | 0.11 |
| TNF | -0.01 | 0.66 | -0.09 | 0.65 |
| IFN-$\gamma$ | 0.42 | 0.06 | 0.31 | 0.12 |

表 28　複迴歸分析探討 B 廠勞工各影響因子與細胞激素之相關性

| 模式 | 未標準化之係數 B | 標準誤 Std. Error | 標準化後係數 Beta | T-值 | p-value |
|---|---|---|---|---|---|
| LogIL-2 | | | | | |
| 常數項 | 4.75 | 3.8 | 0 | 1.25 | 0.23 |
| 吸菸習慣 | -0.42 | 0.49 | -0.2 | -0.86 | 0.4 |
| 籍貫 | 0.9 | 1.34 | 0.2 | 0.68 | 0.51 |
| 年齡(年) | -0.08 | 0.06 | -0.32 | -1.36 | 0.2 |
| 矽肺症 | 1.13 | 0.5 | 0.55 | 2.28 | **0.04** |
| BMI | -0.004 | 0.1 | -0.01 | -0.03 | 0.97 |
| LogIL-4 | | | | | |
| 常數項 | 0.56 | 0.81 | 0 | 0.7 | 0.5 |
| 吸菸習慣 | 0.07 | 0.11 | 0.16 | 0.65 | 0.53 |
| 籍貫 | 0 | . | . | . | . |
| 年齡(年) | -0.006 | 0.009 | -0.19 | -0.73 | 0.48 |
| 矽肺症 | -0.04 | 0.11 | -0.1 | -0.38 | 0.71 |
| BMI | 0.02 | 0.02 | 0.22 | 0.89 | 0.39 |
| LogIL-6 | | | | | |
| 常數項 | 0.41 | 1.6 | 0 | 0.26 | 0.8 |
| 吸菸習慣 | 0.23 | 0.27 | 0.21 | 0.85 | 0.41 |
| 籍貫 | -0.65 | 0.76 | -0.25 | -0.86 | 0.4 |
| 年齡(年) | -0.004 | 0.02 | -0.05 | -0.19 | 0.85 |
| 矽肺症 | 0.03 | 0.28 | 0.02 | 0.09 | 0.93 |
| BMI | 0.05 | 0.06 | 0.24 | 0.86 | 0.4 |
| Log IL-10 | | | | | |
| 常數項 | 1.82 | 0.98 | 0 | 1.86 | 0.08 |
| 吸菸習慣 | -0.04 | 0.16 | -0.06 | -0.29 | 0.78 |
| 籍貫 | 0.45 | 0.45 | 0.24 | 0.99 | 0.34 |
| 年齡(年) | -0.02 | 0.01 | -0.3 | -1.37 | 0.19 |
| 矽肺症 | 0.46 | 0.16 | 0.62 | 2.77 | **0.01** |
| BMI | -0.04 | 0.03 | -0.28 | -1.16 | 0.26 |
| LogTNF | | | | | |
| 常數項 | 1.76 | 0.87 | 0 | 2.02 | 0.06 |
| 吸菸習慣 | 0.15 | 0.14 | 0.25 | 1.04 | 0.32 |
| 籍貫 | 0.28 | 0.4 | 0.21 | 0.7 | 0.49 |
| 年齡(年) | -0.01 | 0.01 | -0.24 | -0.97 | 0.35 |
| 矽肺症 | 0.23 | 0.16 | 0.39 | 1.43 | 0.17 |
| BMI | -0.04 | 0.03 | -0.38 | -1.26 | 0.23 |

| | | | | | |
|---|---|---|---|---|---|
| LogIFN-$\gamma$ | | | | | |
| 常數項 | 2.16 | 1.78 | 0 | 1.22 | 0.24 |
| 吸菸習慣 | 0.14 | 0.3 | 0.11 | 0.48 | 0.64 |
| 籍貫 | 1.12 | 0.84 | 0.38 | 1.33 | 0.2 |
| 年齡(年) | 0.003 | 0.02 | 0.03 | 0.11 | 0.91 |
| 矽肺症 | -0.17 | 0.32 | -0.14 | -0.52 | 0.61 |
| BMI | -0.07 | 0.06 | -0.31 | -1.12 | 0.28 |

註解：未吸菸比吸菸；閩南以外比上閩南；以 ILO 1/0 以上作為判斷有矽肺症之依據

附錄一　鑄造廠作業員工健康調查問卷

附錄二　期刊論文

## 附錄一：鑄造廠作業員工健康調查問卷

### 一、基本資料

填 寫 時 間：　　年　　月____日
性 別：☐①男 ☐②女
廠 別：☐①精鍊廠 ☐②　　廠 ☐③　　廠 ☐④其它：　　廠
工 號：
出 生：民國　　年　　月　　日
家中電話：（____）_____ 手機：
籍　貫　別：　☐①閩南人 ☐②客家人 ☐③原住民同胞　☐④外省籍 ☐⑤泰國籍 ☐⑥菲律賓籍　☐⑦越南籍　☐⑧其他：
教 育 程 度：　☐①未受正規教育 ☐②小學 ☐③國(初)中　☐④高中（職）☐⑤大專以上
婚 姻 狀 態：　☐①未婚 ☐②已婚 ☐③離婚 ☐④喪偶
身高:_____公分，體重:_____公斤

### 二、工作史

1.民國____年____月進入本廠工作。
2.目前擔任的**工作項目**是☐①造模區 ☐②噴模區 ☐③核模區 ☐④電爐區 ☐⑤澆鑄區 ☐⑥拆模區 ☐⑦噴砂區　☐⑧研磨區 ☐⑨成品放置區 ☐⑩行政人員 ☐11.清潔人員 ☐12.其它（請詳述_____），自民國____年____月從事此工作。
3.您是☐①**固定班**（☐❶早班: 早上 7 點-下午 3 點　☐❷晚班: 下午 3 點- 晚上 11 點 ☐❸大夜班: 晚上 11 點- 隔天早上 7 點）
☐②**輪班制**（班別為: ☐❶甲班　☐❷乙班　☐❸丙班）
☐③**常日班**（早上 7 點 50 分-下午 5 點 30 分）

4.您曾在**本廠其他部門**工作過嗎？
☐①是　☐②否（答「**是**」者，請繼續回答框內問題）

| 工作期間 | 工作內容(填入第 2 題之代號) | 在您的工作場所是否會接觸或用到以下的物質，**請打√**，若知道名稱**請說明** | | | | |
|---|---|---|---|---|---|---|
| | | 粉塵 | 金屬燻煙 | 噪音 | 高溫 | 其他（請說明項目） |
| ❶自民國___年___月至民國___年___月 | | | | | | |
| ❷自民國___年___月至民國___年___月 | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| ❸自民國___年___月<br>至民國___年___月 | | | | | | |

5.您曾在**本廠以外之工廠或公司**工作過嗎？(每週 30 小時以上、工作半年以上之經歷)

☐①有　　☐②沒有（答「**有**」者，請繼續回答框內問題）

| 工作場所 | 工作項目 | 期間(**年**) |
|---|---|---|
| 採石場 | | |
| 煤礦場 | | |
| 鑄造(翻砂)廠 | | |
| 家庭紡織代工 | | |
| 陶瓷廠 | | |
| 石綿廠 | | |
| 拆船修船廠 | | |
| 其他:<br>(請說明) | | |

6.您在本廠工作時，有使用**個人防護具**嗎？

☐①有　　☐②沒有（答「**有**」者請繼續回答框內問題，並於適當處打✓）

| 防護具使用情形 | 棉質口罩 | 防塵口罩 | 耳 塞（罩） | 膠質手套 | 手 套（棉） | 工作衣（布質） | 其他（請說明項目） |
|---|---|---|---|---|---|---|---|
| ❶從未穿戴使用 | | | | | | | |
| ❷偶而穿戴 | | | | | | | |
| ❸大約有一半工作時間使用 | | | | | | | |
| ❹使用超過一半工作時間 | | | | | | | |
| ❺工作時都有穿戴使用 | | | | | | | |

## 三、自覺症狀及過去病史

（一）您有沒有下列症狀，請依**症狀發生情形**在空格內打✓

| | 症　狀 | 未曾發生 | 偶爾發生 | 有時發生 | 常常發生 |
|---|---|---|---|---|---|
| ❶ | 關節腫脹或疼痛，關節炎 | | | | |
| ❷ | 下背痛(背部疼痛) | | | | |
| ❸ | 發 燒(自覺體溫升高) | | | | |
| ❹ | 重 聽(聽力變差) | | | | |
| ❺ | 皮膚過敏(癢或起疹子) | | | | |
| ❻ | 喉嚨刺激感 | | | | |
| ❼ | 反覆性喉嚨痛 | | | | |
| ❽ | 鼻塞 | | | | |
| ❾ | 結膜炎(眼睛紅腫癢痛) | | | | |

（二）下面要請教您一些與您的胸部健康有關的問題，請儘可能以您所知回答「**是**」或「**不是**」，假如您**不能確定問題的答案**為「是」或「不是」，則勾選「**不是**」。

1. 您經常有**胸悶或呼吸短促**的情形嗎?（所謂「胸悶」是指胸部沉重或緊縮的感覺，「呼吸短促」是指呼吸速度比正常還快且短）

☐①是

→ ❶像上面所形容的胸悶**或**呼吸短促，通常在什麼時候發生? ☐①偶爾在開始上班第一天會發生 ☐②幾乎每次開始上班第一天發生且只有第一天發生 ☐③開始上班第一天及其他天也有發生 ☐④和上班無關

❷您經常的胸悶**或**呼吸短促有多少年？_____年

☐②不是

2. 咳嗽

①您通常會**咳嗽**嗎？（所謂「會咳嗽」指如早上吸第一口香煙時，或剛出門時的咳嗽，而平常清喉嚨的咳嗽則不算）

☐❶是

→ ①您通常咳嗽一天四次到六次或一週四天或四天以上嗎？
☐①是 ☐②不是

☐❷不是

❸您早上起床後是否經常有咳嗽的現象呢？ ☐①是 ☐②不是

❹您白天其他時間或晚上是否經常有咳嗽的現象？ ☐①是 ☐②不是

**上述 ❶~❹題若有任一答案為「是」，繼續回答下列問題，假如都答「不是」者，請跳至第3題回答**

❺您在上班時才會(或加重)咳嗽嗎? ☐①是 ☐②不是

❻像上面所形容的咳嗽，您是不是每天都有，而且一年間連續三個月以上？
☐①是 ☐②不是

❼您有這樣的咳嗽多少年？_____年

3.有關咳「痰」情形

①您經常**有痰從胸部咳出來**嗎？（吸第一支煙或剛出門的痰要算，吞下的痰要算，從鼻子出來的痰不算）。

☐❶是

→ ①您經常一天有二次或二次以上，或一週有四天或四天以上的咳痰嗎？
☐①是　☐②不是

☐❷不是

❸您早上起床或清晨第一件事經常是咳痰嗎？　☐①是　☐②不是

❹除早上起床外，您在白天或晚上休息時經常咳痰嗎？　☐①是　☐②不是

**上述問題（從❶-❹題）有任一題答「是」者，繼續回答下列問題，假如都答「不是」者，請跳至第 4 題回答**

❺您在上班時才開始(或加重)吐痰嗎?　☐①是　☐②不是

❻像上面所形容的吐痰情形，您是否幾乎每天都有，且在一年間連續三個月以上嗎？　☐①是　☐②不是

❼您這樣的吐痰有多少年了？ _____年

4.咳嗽及吐痰症狀發生次數

①您是否有一段時期**咳嗽及咳痰**在一年中持續達三個月或更久的情形？（如果您通常就有咳嗽及吐痰的症狀，那麼本題是問您這 2 種症狀是否有增加的現象）

☐❶是

→ ①您在一年中咳嗽及吐痰長達三個月之久的情形有多少年？
_____年

☐❷不是

5.喘鳴

①您的胸部有過**喘鳴或氣喘性**的聲音（俗稱嘎龜ㄏㄟ ㄍㄨㄟ）嗎？

❶當您感冒時　☐①有 ☐②沒有

❷除了感冒外有時會發生　☐①有 ☐②沒有

❸大多數白天或晚上　☐①有 ☐②沒有

**❶❷❸任何一項答「有」者，接答②題，否則跳至第 6 題**

②您有這樣的喘鳴有多少年？　_____年

6.您曾經有過因喘鳴而引起呼吸短促的現象嗎？

☐①有

→ ❶您第一次有這種喘鳴及呼吸短促的現象是發生在您幾歲時？ _____歲
❷您已經有二次或二次以上類似的症狀嗎？　☐①有 ☐②沒有
❸您曾經因為這些症狀而必須服藥或治療嗎？　☐①有 ☐②沒有

☐②沒有

7.呼吸困難

①您是否（除了心或肺的疾病外）有任何情況會引起您無法走動嗎？

☐❶是　（請詳述當時情況_____）**請跳至第 8 題回答**

☐❷不是 **（請繼續回答）**

②在平地快速行走或爬上小山坡時，您有過**呼吸困難**的情形嗎？

☐❶有

①當您與同年齡的人在平地上行走時，您會因呼吸困難而步伐較慢嗎？
☐①會　☐②不會

②以您自己的步伐在平地上行走時，會因呼吸困難而必須停下來休息嗎？
☐①是　☐②不是

③您在平地走了大約 100 公尺(或數分鐘)後，是不是必須停下來休息呢？
☐①是　☐②不是

④您更換衣服是不是會覺得呼吸困難或因呼吸困難而不能外出走動？
☐①是　☐②是

☐❷沒有

8. 感冒及胸部疾病

①如果您曾感冒過，是否**感冒經常會影響您的胸部**，而使您感到不舒服(「經常」乃指平均每二次感冒至少有一次會發生胸部症狀)　☐①是　☐②不是

②過去三年來您是不是曾經**因胸部疾病而暫停工作一日以上**，在家療養或住院？

☐❶是

①當您患有上述的胸部疾病時，是不是有咳痰的現象？ ☐①是 ☐②不是
②過去三年來有多少次類似的胸部疾病，使您痰（或痰增加）持續了一個星期或更久？　☐①有____次胸部疾病　☐②沒有此種胸部疾病

☐❷不是

**（二）過去病史**

1. 在 **16 歲以前**您曾有過肺部疾病嗎？　☐①有　☐②沒有　☐③不記得

2. 您**曾得過下列疾病**嗎？

①**急性支氣管炎**　☐❶是

①您初次得到支氣管炎是幾歲？____歲
②是由醫師診斷確定的嗎？　☐①是　☐②不是

☐❷不是

②**肺炎（包括支氣管肺炎）**☐❶是

①您初次得到肺炎是幾歲？____歲
②是由醫師診斷確定的嗎？ ☐①是　☐②不是

☐❷不是

③**慢性支氣管炎** （一年內連續三個月以上的咳嗽及咳痰，且連續兩年以上）

☐❶是

①您初次得到慢性支氣管炎是幾歲？ _____歲

②是由醫師診斷確定的嗎？ □①是 □②不是
③您現在還有這個病嗎？ □①是 □②不是

□❷不是

④**肺氣腫** □❶是

①您初次得到肺氣腫是幾歲？____歲
②是由醫師診斷確定的嗎？ □①是 □②不是
③您現在還有這個病嗎？ □①是 □②不是

□❷不是

⑤**氣喘** □❶是

①您初次得到氣喘是幾歲？____歲
②是由醫師診斷確定的嗎？ □①是 □②不是
③您現在還有這個病嗎？ □①是 □②不是，那麼____歲痊癒的
④您現在須要用藥物治療嗎？ □①是 □②不是
⑤進入紡織廠工作以前您是否有氣喘疾病？ □①是 □②不是

□❷不是

⑥**過敏性鼻炎** □❶是

①您初次得到此病是幾歲？____歲
②是由醫師診斷確定的嗎？ □①是 □②不是

□❷不是

⑦**胸膜炎** □❶是

①您初次得到此病是幾歲？____歲
②是由醫師診斷確定的嗎？ □①是 □②不是
③您現在還有這個病嗎？ □①是 □②不是，那麼____歲痊癒的

□❷不是

⑧**肺結核** □❶是

①您初次得到此病是幾歲？____歲
②是由醫師診斷確定的嗎？ □①是 □②不是
③您現在還有這個病嗎？ □①是 □②不是，那麼____歲痊癒的

□❷不是

3. 您曾經有過

①任何**上述 8 種疾病以外的胸部疾病**嗎？

□❶有(請寫出病名_____)

□❷沒有

②任何的**胸部手術**嗎？

□❶有(請寫出病名_____)

☐❷沒有

③是否有醫師曾經告訴您有**心臟疾病**嗎？

☐❶有

→ 在過去十年中您曾經因心臟疾病而接受過治療嗎？
☐①有　　☐②沒有

☐❷沒有

④是否有醫師曾經告訴您有**高血壓**嗎？

☐❶有

→ 在過去十年中您曾經因高血壓而接受過治療？
☐①有　　☐②沒有

☐❷沒有

## 四、家族史

（一）您雙親中是否有任何一個曾經由醫師證實患有**慢性肺部疾病**嗎？

| | **父親** | **母親** |
|---|---|---|
| ①慢性支氣管炎 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |
| ②肺氣腫 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |
| ③氣喘 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |
| ④肺癌 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |
| ⑤肺結核 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |
| ⑥其他胸部疾病 | ☐❶是 ☐❷不是 ☐❸不知道 | ☐❶是 ☐❷不是 ☐❸不知道 |

（二）您的雙親**仍健在**嗎？

| | |
|---|---|
| ☐①是　（現在_____歲） | ☐①是　（現在_____歲） |
| ☐②不是（死亡年齡____歲，或 | ☐②不是（死亡年齡____歲，或 |
| ③☐不知道死亡年齡） | ③☐不知道死亡年齡） |
| 請寫出**死亡原因**_____ | _____ |

## 五、吸煙狀況

1. 您曾經**吸煙**嗎？（**一生中**如有下列三種情況之一者，請答「**不是**」）

①少於 300 公克（半台斤）之煙草　②少於 20 包香煙　③一年間小於每天一根香煙

☐①是

→ ❶您現在抽煙嗎？（一個月前仍未戒掉才算）☐①是　☐②不是
❷您幾歲開始習慣性地抽煙？____歲
❸假如您已經完全戒煙，請問是在幾歲戒掉？_____歲，共抽_____年

❹那您戒煙前那段日子平均每天抽多少支？____支
❺假如您現在還在抽煙，那麼通常每天抽多少支？每天____支
❻您過去或現在抽煙時把煙吸入肺部嗎？
□①從來沒有 □②輕微吸入 □③中度吸入 □④重度吸入

□②不是

2.請問您有無**嚼檳榔**習慣（從開始嚼到現在已超過50顆）
1.□無
2.□有(請在下列**I.II.III.三項中擇一**回答)
Ⅰ.□每天嚼檳榔：平均一天約嚼____顆，已嚼多久____年____月
Ⅱ.□偶而嚼檳榔：平均一週約嚼____顆，已嚼多久____年____月
Ⅲ.□已不嚼檳榔：最後一次規律嚼檳榔（每天有嚼1顆以上）距今約多久？
1.□0-1月 2.□1-3月 3.□3-6月 4.□6-12月 5.□1-5年
6.□5-15年 7.□15年以上 8.□不曾規律嚼檳榔
主要嚼檳榔種類為何？
1.□荖花（藤）檳榔（菁仔＋荖花＋熟石灰＋紅灰）
2.□葉檳榔（菁仔＋荖花（藤）＋石灰）
3.□荖藤檳榔（菁仔＋硬荖藤＋白灰）
4.□其他_____

# 附錄二　期刊論文

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ORIGINAL ARTICLE

# An engineering intervention resulting in improvement in lung function and change in urinary 8-hydroxydeoxyguanosine among foundry workers in Taiwan

**Ming-Hsiu Lin · Saou-Hsing Liou · Ching-Wen Chang · I-Hsiao Huang · Paul T. Strickland · Ching-Huang Lai**

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**Abstract**
*Purpose* To assess changes in oxidative DNA damage and lung function amongst a group of foundry workers resulting from an engineering intervention to reduce air respirable dust in their working environment.
*Methods* We studied all 22 workers recruited from a typical small Taiwanese iron foundry plant before and 3 months after improvements to air exhaust control. The effectiveness of the air exhaust intervention in reducing respirable dust and $SiO_2$ was determined by personal breathing-zone air sampling. Initial baseline biomarker measurements were taken of lung function and urinary 8-hydroxy-deoxyguanosine (8-OHdG) in all of the workers, with follow-up measurements taken 3 months after the engineering control was put in place. Generalized estimating equations were used to assess the effect of the intervention on lung function and oxidative DNA damage.
*Results* Following the intervention, respirable dust density decreased from $2.87 \pm 1.38$ mg/m$^3$ to $1.60 \pm 0.70$ mg/m$^3$ ($p = 0.07$), and $SiO_2$ concentration decreased from $0.43 \pm 0.25$ mg/m$^3$ to $0.18 \pm 0.11$ mg/m$^3$ ($p < 0.05$). Compared to initial baseline, significant improvements were found in lung function (FVC, FEV1, FVC%pred and FEV1%pred) amongst the workers after the engineering intervention. A significant increase in concentration of urinary 8-OHdG was observed after the engineering intervention in smokers, but not in non-smokers.
*Conclusions* These findings indicate that reductions in workplace respirable dust and $SiO_2$ concentration can result in improved lung function amongst foundry workers.

**Keywords** Foundry workers · 8-hydroxydeoxyguanosine · Lung function · Engineering intervention

M.-H. Lin
Institute of Occupational Safety and Health, Council of Labour Affairs, Executive Yuan, Taipei 221, Taiwan, R.O.C

S.-H. Liou · C.-H. Lai (✉)
Department of Public Health, National Defence Medical Center, Taipei 114, Taiwan, R.O.C
e-mail: lgh@mail.ndmctsgh.edu.tw

M.-H. Lin · C.-W. Chang
Institute of Environmental Health, National Taiwan University, Taipei, R.O.C

I.-H. Huang
Center for Environmental Safety and Health Technology Development, Taipei, R.O.C

S.-H. Liou
Division of Environmental Health and Occupation Medicine, National Health Research Institute, Miaoli County 350, Taiwan, R.O.C

P. T. Strickland
Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

## Introduction

Occupational exposure to foundry moulds containing silica has been reported to cause respiratory diseases and impaired lung functioning. Crystalline silica is a major component of the sand widely used in moulds in the foundry industry. The International Agency for Research into Cancer (IARC 1997) concluded that there is sufficient evidence in humans to classify crystalline silica as a human carcinogen. Epidemiological and pathological studies suggest that, even in the absence of radiological signs of silicosis, silica dust exposure can lead to chronic

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obstructive pulmonary disease (Hnizdo and Vallyathan 2003; Ulvestad et al. 2001). Furthermore, the association between cumulative silica dust exposure and airflow obstruction is independent of any diagnosis of silicosis (Forastiere et al. 2002; Liou et al. 1996).

A strong relationship has been demonstrated between dust exposure levels and respiratory abnormalities within the iron foundry industry, where cumulative exposure to dust is found to cause accelerated degradation in lung functioning (Kuo et al. 1999). One study reported a 1.45-fold increase in the risk of developing a radiograph consistent with that of silicosis after 20 years of work, and a 2.10-fold increase in such risk after 40 years of work (Rosenman et al. 1996). As in the case of pneumoconiosis, silicosis arising from the inhalation of dust containing crystalline silica is irreversible, but nevertheless preventable.

There is an urgent need for better exposure controls in Taiwan where the majority of the foundry plants are small enterprises (with an average of less than 50 employees). From a survey of health hazards faced by foundry workers in central Taiwan, Kuo et al. (1999) found an overall pneumoconiosis prevalence rate amongst males of 8.8%, with the highest levels being discernible amongst furnace workers (16.3%) and after-processing workers (11.4%), and the lowest levels being found amongst administrative staff (2.5%).

Improvements in the control of the hazards outlined earlier clearly represent the most efficient way of reducing silica exposure. The primary aim of this study was to evaluate changes in lung function and oxidative damage markers following the introduction of an engineering control intervention designed to reduce levels of respirable dust. Exposure was assessed through the use of respirable particle and silica concentration measures, whilst urinary 8-hydroxy-deoxyguanosine (8-OHdG) was used as a measure of oxidative DNA damage. We assessed changes in lung function as a health outcome related to the engineering intervention.

## Materials and methods

### Study population

This longitudinal study was carried out amongst foundry workers with occupational exposure to free silica. Study participants provided signed informed consent prior to enrolment. The study was approved by the institutional review boards at the Tri-Services General Hospital, Taipei, Taiwan. The population recruited for the study comprised all workers employed within a foundry plant located in northern Taiwan. This foundry was a typical small Taiwanese iron foundry plant, with a total of 22 workers, and engaged in iron casting. The plant had not implemented any educational training relating to hazardous dust and had not provided any personal respiratory protection to workers. The engineering intervention (described below) was undertaken in the workshops of the foundry plant.

### Outcome assessment

The outcomes of interest were oxidative DNA damage, using the concentration of 8-OHdG in urine as the biomarker, and workers' lung function using standard spirometry measures. The analysis and assessment of the changes in these two indicators were determined before and 3 months after the air control engineering intervention in their working environment. In order to take into account the stage of any prevalent pneumoconiosis, chest X-rays were taken at baseline.

### Description of engineering control intervention

This study focuses on engineering improvements in specific work areas of the foundry characterized by high dust exposure, including the sand pouring/shake out area, the particulate collection device location and the waste areas (Fig. 1). Although the use of water is normally prohibited in the foundry process, this intervention included the use of two water spray devices as a means of reducing dust

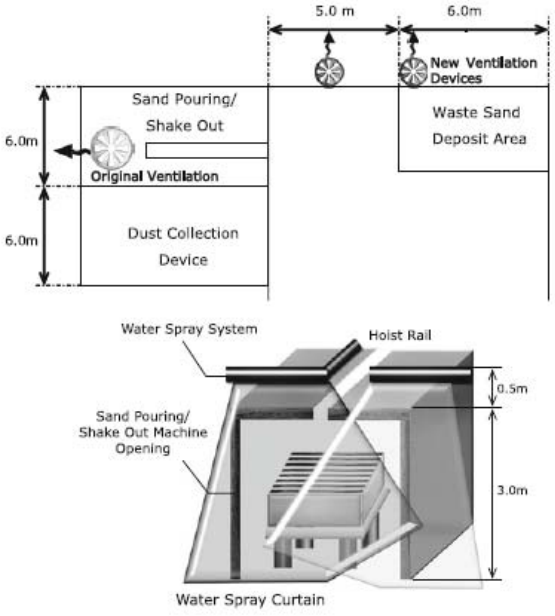


**Fig. 1** Engineering improvement planning and water spray deployment in foundry

exposure. A 3-metre tall water spray system was installed at the inlet/outlet point of the sand pouring/shake out machine, with an additional water spray system installed in the waste sand deposit area. The specifications of the water spray system included a nozzle diameter of 0.3 mm, with a total of 100 nozzles, each with a water flow rate of 100 mL per minute. Each water spray system had its own motor with a pressure of 50–70 kg/cm$^2$ and total water flow of 10 L per minute. In addition to the water spray devices, two wall-mounted industrial fans, 1.2 m in diameter, were installed to bring clean external air into the areas of higher dust exposure in order to reduce the overall exposure levels of the workers (Fig. 1).

## Data and sample collection

Self-administered questionnaires were distributed to the participants, at both baseline and follow-up time points of the study, requesting details of personal characteristics, such as age, education, alcohol consumption, smoking, daily dietary intake, use of vitamin supplements and use of personal protective equipment.

Workers were asked to collect a spot urine sample in a container provided and were given a chest radiography examination and a lung function test at baseline. Lung function testing and 8-OHdG measurements were repeated 3 months after the workplace intervention was into operation. Personal breathing-zone air samples were collected from the study subjects by battery-operated personal air-sampling pumps at baseline and follow-up periods of the study.

## Respiratory particulate sampling

Personal breathing-zone air samples were collected from the subjects by battery-operated personal air-sampling pumps. In addition, environmental air samples were collected according to different job categories. The measurements of the respirable dust fraction are conducted using a cyclone pre-selector to collect a 50% (or median) cut-point for a respirable particulate matter sampler of 3.5 μm. The samplers were comprised of a 10-mm diameter nylon cyclone (SKC, 80061, USA), a PVC membrane filter (5-μm pore size, 37-mm diameter) and a pump (Gilian, Air-5, USA). The low-ash 5-micron PVC filter is the preferred sampling medium for respirable dust containing crystalline silica and is used in the American Industrial Hygiene Association (AIHA) Performance Analytical Testing (PAT) Program. The 5-micron pore size filters reduce problems associated with sample loading and back pressure. This condition is important to maintaining a constant sampling rate in dusty work environments (Rappaport et al. 2003). The pre-calibrated battery-operated air-sampling pumps were adjusted to operate at a flow rate of 1.7 L per minute, recalibrated both before and after each sampling session with a Minibuck soap bubble airflow calibrator for a sampling duration of about 6 h.

In addition to the samples collected, unexposed filters (10%) were submitted for analysis as field blanks. The gravimetric analysis was conducted inside a constant 60% relative humidity weighing chamber using a microbalance (Mettler-Toledo, MT5, Greifensee, Switzerland) with 1 μg sensitivity. Prior to its daily usage, the microbalance was calibrated with manufacturer-supplied traceable calibration weights. All of the filters were conditioned for at least 24 h prior to weighing and were passed over a static neutralizer (Allfield, Taipei, Taiwan) to reduce any filter electrostatic charge which could potentially interfere with the accuracy of the gravimetric analysis.

## Crystallite silica analysis

The samples were analysed according to NIOSH 7602 methodology using X-ray diffraction (XRD) (Rigaku, GN 4013A1). The filter paper containing respirable dust was incinerated for 1 h at 800°C, and the ashes dissolved in an isopropyl alcohol solution. This suspension was then filtrated with silver filter paper and analysed using XRD. The QA/QC procedures of the crystalline free silica indicated precision of 3.5%; accuracy of 4.0%; an $r^2$ value of 0.993; a quantification limit of 2.8 μg; and recovery efficiency rates of $98.4 \pm 2.1\%$ (standard) and $97.1 \pm 8.4\%$ (samples).

## Urinary 8-OHdG analysis

Levels of urinary 8-OHdG were determined by indirect competitive enzyme-linked immunosorbent assay (ELISA) in accordance with the new 8-OHdG Check (Institute for the Control of Aging, Fukuroi, Shizuoka, Japan) as reported by Chuang et al. (2003). The urine samples were thawed and centrifuged at 2,000 rpm for 10 min in order to clarify the samples prior to assay. Sample (50 μl) or standard and primary monoclonal antibodies (50 μl) were added to microtiter plates that had been pre-coated with 8-OHdG. The plates were subsequently incubated at 37°C for 1 h with continuous mixing at 100 rpm.

After washing the wells with 250 μl phosphate-buffered saline (PBS), 100 μl horseradish peroxidase (HRP)-conjugated secondary antibodies was added to each well, and the plates were incubated for 1 h with mixing. The unbound secondary antibody was removed by washing with PBS as above. Chromatic substrate (100 μl) was then added to each well, and the plates were incubated in the dark at room temperature for 15 min. Phosphoric acid (100 μl of 1.0 M) was then added to terminate the reaction.

The absorbance was measured at 450 nm with a computer-controlled ELISA reader (MRXII, Dynex Technologies, VA, USA); the concentration of 8-OHdG in the urine samples was interpolated from a standard curve. Throughout the period of our sample analysis, the coefficient of variation of the assay was 6%. The results are expressed as μg/g creatinine.

### Determination of pulmonary function

A portable spirometer (HI-701, Japan) was used to perform the forced expiratory measurements. The lung function values were also expressed as a percentage of the predicted values according to the age, gender, height and weight of the individual. The lung function measurements were carried out in a standardized manner in accordance with the guidelines of the American Thoracic Society (ATS). The measurements included in the analysis were those in which the two highest attempts were within 5% agreement with the ATS criteria.

The lung functioning parameter analyses included 'forced vital capacity' (FVC); 'forced expiratory volume exhaled in the first second' (FEV1); the ratio of FEV1 to FVC expressed as a percentage (FEV1/FVC%); the ratio of FVC to FVCpred expressed as the percentage of the predicted value for the age, gender, height and weight of the individual (FVC%pred); and the ratio of FEV1 to FEV1pred expressed as a percentage (FEV1%pred). The lung function prediction equations are based on Asian male models, FVC (ml) = (27.63 − 0.112*age)*height, FEV1 (ml) = 34.4*height − 33*age − 1,000.

### Statistical methods

Our analysis began with a comparison of the post hoc distributions of lung function and 8-OHdG concentrations between the before and after intervention measurements, assessing the difference between the means using paired *t*-tests and comparing the distributions using the non-parametric Wilcoxon rank-sum test.

The relationships between cumulative exposure to dust, urinary 8-OHdG concentrations and lung function were also examined using multiple regression models. The covariates used in all of the analyses included BMI and smoking status. The lifetime cumulative exposure variables were fitted so as to describe the exposure concentration multiplied by the service duration in years. We assessed the determinants of lung function and 8-OHdG levels using the method of generalized estimating equations (GEE), which accounted for correlated successive measurements on the same individuals. All of the analyses in this study were performed using the STATA 8 statistical package.

## Results

### Study population characteristics

The mean age of the foundry workers was 44.3 years (SD 11.2), and the mean duration of work was 13.3 years (SD 18.3) (Table 1). The most common job categories were pattern making (41%) and moulding (45%). More than half of the subjects (55%) were current smokers. Seven subjects presented with ILO X-ray classifications of 1/0 or 1/1.

### Dust sampling and crystallite silica analysis

Dust sampling and crystallite silica analysis were undertaken at both baseline and follow-up. As shown in Table 2, the mean concentration of total respirable dust was 2.87 mg/m$^3$ (SD 1.38) at baseline and 1.60 mg/m$^3$ (SD 0.70) at follow-up after 3 months of intervention ($p = 0.07$ Wilcoxon sign rank test). Similarly, the mean concentration of respirable crystallite silica was 0.43 mg/m$^3$ (SD 0.25) at baseline and 0.18 mg/m$^3$ (SD 0.11) at follow-up ($p \leq 0.05$ Wilcoxon sign rank test).

### Pulmonary function and urinary 8-OHdG

Comparing pulmonary function and urinary 8-OHdG between baseline and follow-up indicates significant

**Table 1** Study population characteristics

| Characteristics | No. | % |
|---|---|---|
| Age[a] | 44.3 ± 11.2 | |
| BMI (kg/m$^2$)[a] | 25.17 ± 3.09 | |
| Duration of service[a] | 13.3 ± 18.3 | |
| Education | | |
| <High school | 13 | 59.1 |
| ≥High school | 7 | 31.8 |
| Missing value | 2 | 9.1 |
| Type of job category | | |
| Pattern making | 9 | 40.9 |
| Coating | 2 | 9.1 |
| Moulding | 10 | 45.5 |
| Pattern & moulding | 1 | 4.5 |
| Current smoking habit | | |
| Smoker | 12 | 54.5 |
| Non-smoker | 10 | 45.5 |
| X-ray classification | | |
| ILO (0/0) | 15 | 68.2 |
| ILO (1/0) | 5 | 22.7 |
| ILO (1/1) | 2 | 9.1 |

*BMI* Body mass index, *ILO* International labour organization

[a] Mean ± SD

**Table 2** Exposure and effect measurements at baseline and follow-up in foundry workers

| Exposure and effects | Baseline | Follow-up | $p$ value[a] |
|---|---|---|---|
| Exposure | | | |
| Respirable dust density ($mg/m^3$) | 2.87 ± 1.38 | 1.60 ± 0.70 | 0.07 |
| $SiO_2$ ($mg/m^3$) | 0.43 ± 0.25 | 0.18 ± 0.11 | <0.05 |
| Effect | | | |
| FEV1(L) | | | |
| Smoker | 2.87 ± 0.98 | 3.59 ± 1.01 | 0.12 |
| Non-smoker | 3.18 ± 0.55 | 4.09 ± 0.52 | <0.05 |
| Subtotal | 3.02 ± 0.74 | 3.87 ± 0.86 | <0.05 |
| $p$ value[b] | 0.25 | 0.18 | |
| FVC(L) | | | |
| Smoker | 3.57 ± 0.90 | 4.45 ± 0.96 | 0.059 |
| Non-smoker | 3.77 ± 0.70 | 4.90 ± 0.62 | <0.05 |
| Subtotal | 3.71 ± 0.76 | 4.73 ± 0.94 | <0.05 |
| $p$ value[b] | 0.424 | 0.183 | |
| FEV1%pred | | | |
| Smoker | 89.6 ± 22.61 | 111.98 ± 24.86 | <0.05 |
| Non-smoker | 93.81 ± 8.13 | 123.01 ± 15.31 | <0.05 |
| Subtotal | 90.95 ± 15.66 | 117.36 ± 20.86 | <0.05 |
| $p$ value[b] | 0.53 | 0.60 | |
| FVC%pred | | | |
| Smoker | 95.54 ± 19.08 | 118.43 ± 21.68 | <0.05 |
| Non-smoker | 97.36 ± 12.43 | 127.47 ± 11.37 | <0.05 |
| Subtotal | 96.97 ± 14.50 | 123.67 ± 18.81 | <0.05 |
| $p$ value[b] | 0.53 | 0.29 | |
| FEV1/FVC% | | | |
| Smoker | 79.12 ± 10.00 | 80.16 ± 6.92 | 0.92 |
| Non-smoker | 84.64 ± 5.60 | 83.70 ± 3.67 | 0.82 |
| Subtotal | 81.12 ± 8.48 | 81.71 ± 6.28 | 0.98 |
| $p$ value[b] | 0.37 | 0.21 | |
| Urine 8-OHdG (ng/ml) | | | |
| Smoker | 8.77 ± 4.89 | 16.39 ± 9.21 | 0.07 |
| Non-smoker | 15.54 ± 15.64 | 11.94 ± 9.47 | 0.46 |
| Subtotal | 12.15 ± 13.83 | 14.17 ± 9.40 | 0.53 |
| $p$ value[b] | 0.62 | 0.31 | |
| Urine 8-OHdG/Cr (μg/g) | | | |
| Smoker | 4.27 ± 3.35 | 9.33 ± 4.23 | <0.05 |
| Non-smoker | 6.03 ± 5.29 | 7.78 ± 5.61 | 0.48 |
| Subtotal | 5.15 ± 4.41 | 8.55 ± 4.91 | <0.05 |
| $p$ value[b] | 0.49 | 0.41 | |

[a] Comparison between the baseline and follow-up periods (Wilcoxon sign rank test)

[b] Comparison between smokers and non-smokers (Kruskal–Wallis test)

improvement in pulmonary function, but 8-OHdG concentration increased only amongst smokers (Table 2). Following the engineering intervention, subjects demonstrated significant increases in FEV1, FVC, FEV1%pred and FVC%pred compared to baseline. In sub-group analysis, these increases were all statistically significant in non-smokers, and significant (FEV1%pred, FVC%pred), or marginally significant (FVC) in smokers. There were no significant differences in FEV1/FVC% between baseline and follow-up.

Amongst non-smokers, there was no significant change in mean concentration of urinary 8-OHdG between baseline and follow-up (Table 2). Amongst smokers, there was a marginal increase in urinary 8-OHdG concentration ($p = 0.07$), that became significant ($p = 0.04$) after creatinine correction. An improvement of lung function test results (28% of FEV1, 30% of FVC, 31% of FEV1%pred for the non-smokers and 25% of FEV1, FVC and FEV1%pred for the smokers) after engineering control. This improvement in lung function between baseline and follow-up resulted in less evidence of deficiencies indicative of possible disease states (Table 3).

At baseline, 5 subjects demonstrated evidence of obstructive or restrictive lung function, whereas at follow-up only 2 subjects demonstrated evidence of pulmonary obstruction.

The relationships between urinary 8-OHdG, lung function and the ad hoc intervention were elaborated using GEE regression analysis, which included adjustments for the potential confounders BMI and age (Table 4). As expected, FEV1 and FVC declined with age. Consistent with the pairwise analysis above, significant improvement in all 4 lung function parameters was observed at follow-up. Comparing follow-up with baseline, there was a 0.103 L increase in logFEV1, a 0.106 L increase in logFVC, a 0.104 L increase in logFEV1%pred and a 0.106 L increase in logFVC%pred after intervention. The increase in creatinine-corrected 8-OHdG concentration after the intervention became marginally statistically significant ($p = 0.08$).

## Discussion

### Respirable dust and silica

The results of this study indicate that, following the engineering intervention, there was a general reduction in air concentrations of dust and silica in the workplace. Although the improvements were focused on specific areas, there were no solid partitions separating different working areas in the foundry, and the dust reduction was apparent throughout the foundry. The mean respirable crystallite silica concentration decreased by 58% from $0.43 \pm 0.25$ $mg/m^3$ at baseline to $0.18 \pm 0.11$ $mg/m^3$ after intervention. Similarly, the mean total respirable dust concentration decreased by 44% from $2.87 \pm 1.38$ $mg/m^3$

**Table 3** Lung function categories at baseline and follow-up

| Analysis variable | Category | Time | |
|---|---|---|---|
| | | Baseline | Follow-up |
| FEV1/FVC ≥ 70%, FVC ≥ 80% | Normal | 17 | 20 |
| FEV1/FVC < 70%, FVC ≥ 80% | Obstructive lung function | 3 (ID = 25, 26, 36) | 2 (ID = 22, 36) |
| FEV1/FVC ≥ 70%, FVC < 80% | Restrictive lung function | 2 (ID = 30, 39) | 0 |
| Total | | 22 | 22 |

*ID* Subject code

**Table 4** Predictors of health outcome in silica-exposed subjects according to generalized estimating equations (GEE) in 22 foundry workers

| Variables | log Urinary 8-OHdG | | log Urinary 8-OHdG/Cr | | logFEV1(L) | | logFVC (L) | | logFEV1%pred | | logFVC%pred | | logFEV1/FVC% | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *β* | *p* value | *β* | *p* value | *β* | *p* value | *β* | *p* value | *β* | *p* value | *β* | *p* value | *β* | *p* value |
| Age (year) | 0.001 | 0.94 | 0.004 | 0.61 | −0.005 | 0.04 | −0.006 | <0.001 | 0.001 | 0.69 | −0.003 | 0.06 | 0.001 | 0.13 |
| BMI (kg/m$^2$) | −0.011 | 0.70 | −0.013 | 0.47 | −0.006 | 0.25 | −0.005 | 0.28 | −0.003 | 0.53 | −0.003 | 0.48 | 0.001 | 0.85 |
| Smoker (Yes/no) | 0.034 | 0.83 | −0.012 | 0.91 | −0.011 | 0.74 | 0.022 | 0.42 | −0.036 | 0.21 | 0.007 | 0.76 | −0.033 | 0.01 |
| Cumulative exposure (mg/m$^3$*year) | −0.001 | 0.93 | −0.006 | 0.42 | 0.001 | 0.70 | 0.001 | 0.48 | 0.001 | 1.00 | 0.001 | 0.69 | 0.001 | 0.92 |
| ILO grade (0/1 above vs 0/0) | −0.356 | 0.16 | −0.271 | 0.11 | 0.010 | 0.84 | 0.057 | 0.18 | −0.008 | 0.86 | 0.046 | 0.21 | −0.048 | 0.02 |
| Time (follow-up vs baseline) | 0.108 | 0.50 | 0.277 | 0.08 | 0.103 | <0.001 | 0.106 | <0.001 | 0.104 | <0.001 | 0.106 | <0.001 | −0.002 | 0.65 |
| Intercept | 1.314 | 0.10 | 0.931 | 0.08 | 0.834 | <0.001 | 0.901 | <0.001 | 2.024 | <0.001 | 2.158 | <0.001 | 1.889 | <0.001 |

*ILO* International labour organization

at baseline to 1.60 ± 0.70 mg/m$^3$ after intervention. The application of water and wall-mounted fans both of which effectively reduced the levels of respirable silica dust are an inexpensive approach for environmental control. However, there are more modern methods for engineering control in the foundries.

## Lung function

We observed significant improvement in lung function measures following the engineering intervention with subjects demonstrating increases in FEV1, FVC, FEV1%pred and FVC%pred compared to baseline. These increases were most consistently demonstrated in non-smokers, presumably due to confounding by cigarette smoke in smokers. Prior studies involving the examination of lung function in foundry workers include the study undertaken by Kuo et al. (1999), who reported an association between cumulative exposure of workers to particulates and decline in lung function. Similarly, these investigators found an association between the exposure of workers to silica dust and decline in lung functioning and increased risk of having silicosis. At baseline, our study identified 5 (of 22) subjects that were classified as having obstructive or restrictive lung function.

## X-ray results

In the GEE analyses, we found FEV1/FVC was significantly reduced with radiography categorized above ILO category 1/0 compared with category 0/0. A consistent result was found for FEV1/FVC ratio—it was decreased in miners with category 2 and 3 (Yang and Lin 2009). Previous studies of the relationship between lung function and silicosis indicate that lung function in subjects with radiographic silicosis (ILO 1/1) is indistinguishable from that of those with ILO 0/0 (Gamble et al. 2004). Slightly greater deficits in lung function were discernible for ILO 3/3 subjects, with more significant degradation in cases with progressive massive fibrosis. Thus, the association between lung function and pneumoconiosis is heavily dependent upon specific pneumoconiosis category. At baseline in our study, two workers could be categorized as possible cases of pneumoconiosis (ILO 1/1) and five workers were designated as radiographic cases (ILO 1/0).

## Urinary 8-hydroxydeoxyguanosine

Exposure to free silica dust leads to lung damage, which induces pneumoconiosis, with the inhalation of crystalline silica potentially producing reactive oxygen species (ROS) (Ding et al. 2002; Fubini and Hubbard 2003; Orman et al. 2005). Attacks on the DNA by ROS result in oxidative DNA damage including the modified base 8-OHdG. Measurement of urinary 8-OHdG in humans has been used as an indicator of oxidative stress and oxidative damage to the DNA (Kelly and Sandstrom 2004; Kim et al. 2004; Pilger et al. 2000; Tokiwa et al. 1999).

We found no significant change in mean concentration of urinary 8-OHdG between baseline and follow-up amongst non-smokers. In smokers, there was a marginal increase in urinary 8-OHdG concentration after the intervention that became significant with creatinine correction. However, since we did not have quantitative measures of smoking at baseline and after intervention, we cannot rule out the possibility that level of smoking changed between the two time points.

Porter et al. (2006) found even after silica exposure has ended, and despite declining silica lung burden, silica-induced pulmonary nitric oxide and ROS production increases, thus producing a more severe oxidative stress. Another explanation may be that oxidative DNA damage is influenced by the interaction between occupational exposures and smoking status (Mukherjee et al. 2004). Smoking foundry workers exhibit a down-regulation in their ability to repair and eliminate damaged DNA compared with non-smokers.

## Possible mechanisms

Sand is the major component used in the moulding process within the foundry industry and is constantly recycled. For the insoluble components of the particles, such as silica, the bio-persistence in the target organ may be expressed as the surface area of the particles multiplied by the surface reactivity; this describes a biologically effective dose which drives the pathogenic effects. However, the very nature of the foundry industry makes it extremely difficult for us to explore whether the associations noted are specific to respirable dust and silica.

From an examination of the relationships between silica exposure, nitric oxide and ROS production, Porter et al. (2002, 2006) found that silica-exposed rat lungs were in a state of oxidative stress, the severity of which increased during the post-exposure period. Similar findings were reported by Knaapen et al. (2002) in rats and by Schins et al. (2002) using A549 culture cells. These studies indicated that DNA strand breakage occurred more readily with exposure to crystallite silica; that is, such exposure leads to the production of more urinary 8-OHdG. Exposure to particulate silica can cause a persistent inflammation sustained by the release of oxidants in the alveolar space (Fubini and Hubbard 2003). The presence of the 8-OHdG in urine represents the primary repair product of oxidative DNA damage in vivo, presumably nucleotide excision repair. Increases in 8-OHdG or other DNA base oxidation products are not necessarily due to increased rates of oxidative DNA damage. It should be emphasized 8-OHdG is also a biomarker reflecting the balance between oxidative damage and repair rate. It is also possible to stimulate DNA repair and therefore decrease steady 8-OHdG concentrations in DNA (Halliwell 2002).

The persistence of particulate silica in the airway may be influenced by rates of uptake, metabolism and clearance. Once in the alveolar space, particles may react with extracellular fluid and be engulfed by alveolar macrophages (AM), which clear the particles out of the lungs. The clearance process may either succeed or fail depending upon the surface characteristics of the particulate silica. The macrophages will be activated at the cellular and molecular level with the activation of transcription factors and the release of oxidants (reactive oxygen species or reactive nitrogen species), proteolytic enzymes, cytokines, growth factors etc., if the clearance process fails (Fubini and Hubbard 2003). Target cells such as bronchiolar and alveolar epithelial cells will be affected by both cellular oxidants (AM products) and noncellular oxidants depending on numerous factors, including silica particle size and surface geometry, as well as inorganic contaminants, particularly iron due to its involvement in Fenton reactions, again resulting in activation and/or cell death (Halliwell 2002).

Porter et al. (2004) have reported results from a rat silica inhalation study which determined that even after silica exposure ended, pulmonary inflammation and damage progressed with subsequent fibrosis development without further silica exposure and in spite of that silica lung burden decreased during recovery. This finding is consistent with the pattern of pulmonary responses reported in humans (Porter et al. 2006). The fibrosis in silica-exposed lungs occurred in the respiratory unit. Silica-induced disease progressed from alveoli containing foci of inflammatory cells during early exposure to fully formed fibrotic nodules. Scabilloni et al. (2005) found silica nodules appear as early as 40 days of silica exposure from a rat inhalation study. After this time point, continued exposure generated a striking increase in the number of fibrotic nodules. Another group of rats was exposed to crystalline silica followed by 36 days of filtered-air exposure also in the same study. The lungs of these animals showed similar increases in fibrotic responses similar to those with continued exposure. That is, the number of nodules for the

filtered-air recovery and nonrecovery group coincided solely with the number of days elapsed from the initiation of silica inhalation rather than the number of days of inhalation exposure. Once nodule formation occurred, at 40 days of exposure, nodules continued to form at the same rate regardless of continuation of silica exposure. It appears that once a threshold for initiation of the fibrotic response is achieved, nodules will continue to grow and proliferate without further exposure (Scabilloni et al. 2005; Porter et al. 2006).

In our study, small numbers of subjects were in the early stage of simple pneumoconiosis. It is reasonable to postulate that the predominant physiological abnormality is airway obstruction because of the reticular nodulation pattern of simple pneumoconiosis on chest radiographs represents the initial stage of dust deposition. The fibrogenic effects of dust on lung parenchyma play a minor role in functional impairment at this stage. The explanation for our finding may be the deposition of dust particles in the airway occurs earlier and faster than in the alveoli. These may form silica macules centred around the walls of terminal bronchioles and obstruct their lumen.

One limitation of this study was the lack of other unmeasured data, such as levels of various kinds of metal fumes, irritant gases, asbestos, carbon monoxide, carbon dioxide, ammonia, HCN, sulphur dioxide, hydrogen dioxide, acrolein, phosphine and phosphorus oxide, formaldehyde, cyanates, etc., in the process for foundry, possibly confounding the results concerning lung function or oxidative stress. Another limitation of this study was the lack of information regarding individual susceptibility in the repair of DNA. A comparison of variation within and between individuals in controlled exposure conditions would provide important insight to the usefulness of 8-OHdG as a biomarker of oxidative stress caused by exposure to foundry pollutants. There is empirical evidence, including genetic and nutritional factors, suggested to influence 8-OHdG metabolism, that was not taken into account in this study (Gromadzinska and Wasowicz 2003).

## Conclusions

We found significant improvements in lung function amongst a small group of foundry workers following the implementation of an engineering intervention that effectively reduced the levels of respirable silica dust. These results suggest that engineering controls aimed at reducing occupational exposure to silica represent an effective approach that may have immediate benefits to workers. Further research is needed to confirm these findings and identify additional biomarkers that can monitor the biological reaction to silica exposure.

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**Conflict of interest** The authors declare that they have no conflict of interest.

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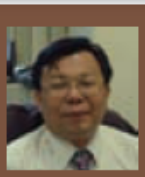
# 鑄造業作業環境改善前後勞工體內氧化性傷害評估



林洺秀[1]


劉紹興[2]


賴錦皇[3]


陳秋蓉[4]

作者：林洺秀[1]、劉紹興[2]、賴錦皇[3]、陳秋蓉[4]
現職：行政院勞工委員會勞工安全衛生研究所[1,4]
國防醫學院公共衛生研究所[2,3]
職稱：副研究員[1]、教授[2]、副教授[3]、組長[4]
TEL：02-26607600 ext.263[1],261[4]、 87923100 ext.18470[2],18464[3]
E-mail：mhlin@mail.iosh.gov.tw[1]、shliou@ndmctsgh.edu.tw[2]、lgh@mail.ndmctsgh.edu.tw[3]、akichn@mail.iosh.gov.tw[4]



本研究主要目的為探討以鑄造工人尿中氧化傷害指標8-OHdG，藉由環境改善或工程改善後作業人員8-OHdG濃度變化情形，以瞭解氧化壓力對DNA造成之氧化傷害情形。

針對高粉塵暴露之作業區，拆模機、集塵設備、廢砂推放區，進行工程改善，配合起重機行徑動線，規劃具簾幕效果之噴水霧裝置。結果顯示介入改善後之環境測定數值已經明顯降低，其可呼吸性結晶型二氧化矽濃度呈現顯著差異；顯示該工程改善已經明顯降低勞工之暴露值。


## 壹、前言

有鑑於塵肺症的職業病給付在我國排行榜是首位，10年來每年都在70%到80%以上。引起塵肺症最主要的原因之一，是吸入含有結晶型游離二氧化矽的粉塵，該粉塵沈積於肺泡中會造成肺部纖維化而產生「矽肺症」(塵肺症之一種)。而美國政府工業衛生師協會(ACGIH, American Conference of Governmental Industrial Hygienists)對於可呼吸性結晶型游離二氧化矽粉塵中石英恕限值(TLV, Threshold Limit Values)為0.05mg/m$^3$， NIOSH之建議濃度亦為0.05mg/m$^3$ (NIOSH, 2000)。若依我國之容許濃度標準規定，假設空氣中粉塵如全為100%結晶型游離二氧化矽時，容許濃度為0.1mg/m$^3$，此為ACGIH及NIOSH所訂定容許濃度值者之兩倍。基於結晶型游離二氧化矽對於肺部之危害，因此國際癌症組織(IARC)，於1997年將結晶型游離二氧化矽之石英與方矽石歸類為Group1(確定人類致癌物質)。

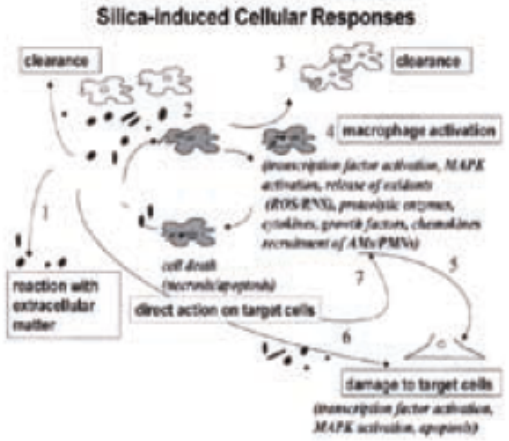



圖1 Silica-induced cellular responses. (1) interaction with extracellular matter, (2) phagocytosis by alveolar macrophage. (AM); (3)clearance; (4) macrophage activation and death; (5) response by target cells to AM products; (6) direct action of the particle on target cells; (7) generation of additional ROS/RNS species.

(From Fubini and Hubbard, 2003)

Fubini及Hubbard以上圖說明暴露二氧化矽後可能引發之細胞反應，首先二氧化矽會於肺泡腔與細胞外反應(步驟一)，誘發肺部巨噬細胞前來進行清除之工作(步驟二)，清除之工作可能成功(步驟三)或失敗(步驟四)，如果是清除失利巨噬細胞會啟動轉錄因子並且釋放活性氧化物(Reactive Oxygen Species) 以及活性氮化物(Reactive Nitrogen Species)，細胞激素、生長因子等最後造成細胞的凋零或死亡以及二氧化矽微粒之釋出；這樣一連串的吞噬、再吞噬將驅使中性白血球、淋巴球，慢性發炎反應因而產生，支氣管或肺部上皮細胞等目標細胞也會受肺部巨噬細胞的產物以及細胞外之二氧化矽微粒所影響導致巨噬細胞之啟動或細胞死亡。Du 和Wang 則探討(2003)二氧化矽可能導致健康的效應，其觀察暴露二氧化矽後之老鼠，由其支氣管肺部之灌洗細胞發現二氧化矽會增加氧氣之消耗，二氧化矽進入到肺泡時，會激發肺部巨噬細胞與表皮細胞形成細胞激素(cytokine)，因而會驅使發炎細胞的產生加強發炎的反應(Interluin-6, IL-6; tumor necrosis factor,TNF-$\alpha$)，另外，亦會引發各種不同的基因產生蛋白質如氧化氮合成酶(inducible NO synthase, iNOS)與 endothelin (ET) 的產生；且巨噬細胞對懸浮微粒會進行胞噬作用，進而產生活性氧化物與活性氮化物。氧化氮合成酶的產生會釋放出大量的一氧化氮。活性氧化物與活性氮化物會對表皮與內皮細胞造成損傷，而造成蛋白質與peptide的不平衡(Ulrich et al., 2002)。另外懸浮微粒上帶有自由基則直接會活化內生性介質，如細胞毒素(cytokines)、腫瘤壞死因子(tumor necrosis factor, TNF)、白血球間素-1(interleukin-1, IL-1)、血小板致活因子(platelet activating factor, PAF)等；這些介質並會進一步誘發宿主產生過量的一氧化氮。

結晶型二氧化矽的暴露除會造成矽肺病，亦可能造成許多自體免疫的疾病以及肺癌；然其致病之分子機轉仍不清楚。儘管如此，發炎反應似乎是暴露二氧化矽後相當常見的初步反應。研究也證實二氧化矽之水溶液會產生$H_2O_2$,HO・,O・,$^1O_2$等自由基(Konecny, 2001)，過量之自由基會造成人體內的氧化傷害。而8-OHdG是一個廣泛被當成活性氧化物種對DNA造成氧化傷害的指標，尿液中8-OHdG的濃度增加與暴露有毒化學物質如多環芳香烴、二氧化矽、抽煙等有關。本研究主要目的為探討以鑄造工人尿中8-OHdG為指標，藉由環境改善或工程改善後作業人員8-OHdG濃度變化情形，以瞭解氧化壓力對DNA造成之氧化傷害情形。

## 貳、研究方法

本研究收集暴露組A、C 兩廠共55 人，A 廠以作業環境改善、C 廠則未採取環境改善措施，並A、C兩廠基準點及作業環境改善後三個月後對兩組進形氧化傷害、指標肺功能測量之檢測。暴露組並進一步按照作業人員之工作類別分成，第一類：造模、噴模、合模；第二類：電爐、澆鑄；第三類：拆模、噴砂、研磨、成品放置、清潔工。

### 一、可呼吸性粉塵結晶型游離二氧化矽分析

以Nylone旋風式10-mm可呼吸性粉塵採樣器(BDX99R, part no.7010048-1 Sensidyne Inc., Largo, FL, 或Part No.456243, MAS, Pittsbsburge, PA, UAS)連接37-mm濾紙採樣匣 (37-mm filter cassette, SKC Inc.) 以封膜 (Sealing band) (Cat.No. 225-25-01, 02, SKC Inc., Eighty Four, PA USA) 封住採樣匣再進行採樣，其所使用採樣介質皆為孔徑0.5$\mu$m 聚氯乙烯濾紙 (PVC, Poly Vinylchloride filter) (Part No. 225-8-01, SKC Inc., Eighty Four, PA USA) 採樣流率1.7 L/min。採樣器之佩帶方式為將PUMP繫於員工後方腰帶上 (以方便員工作業)，再將連接管繞道前方胸前 (左右均可)，將採樣器別於員工衣領上 (為接近呼吸帶處)，將採樣口朝前方，並避免員工遮

蓋住採樣口。可呼吸性粉塵結晶型游離二氧化矽分析依據NIOSH 7500與OSAH ID-142方法，以XRD進行樣本分析。結晶型游離二氧化矽分析係將含可呼吸性粉塵之濾紙樣本置入坩鍋後，以溫度設定於800℃之高溫焚燒爐焚燒2小時。將高溫灰化後之灰分配製成異丙醇懸浮液，並將此溶液過濾於銀膜濾紙，再將製作好的銀膜濾紙樣本以X-光繞射分析(Rigaku, GN4013A1)。

### 二、肺功能測量

肺功能以Microspiro HI-295 (Japan)手提式肺功能機測得，FVC、FEV1及FVC/FEV1等項目。肺功能機微電腦依輸入的年齡、身高、性別資料換算肺功能預期值，其各肺功能之預測值係採東方人種之常模值。在進行測量之前，儀器皆以3公升之唧筒進行校正；與採集尿液同一時間點進行肺功能之測試。

### 三、8-OHdGA之測量方法

本研究參考Yin、劉等人(Yin et al, 1995; 莊等人，2002)發表之酵素結合免疫吸附分析法(enzyme linked immunosorbent assay; ELISA)偵測之。使用OXIS research™ 8-OHdG ELISA試劑組測定，其原理是利用競爭型抑制法的ELISA來偵測8-OHdG，步驟如下：尿液和一次抗體(8-OHdG特定單株抗體)加入已經包覆8-OHdG 的ELISA盤中，37℃反應 1小時，以pH 7.4磷酸鹽緩衝溶液(phosphate buffered saline; PBS)洗掉結合物，加入二次抗體(以山葵根過氧化酶(horseradish peroxidase)標幟之抗球蛋白抗體)，37℃反應1小時後以PBS清洗未結合物，加入呈色劑(3, 3', 5, 5'-tetramethylbenzidine)，避光，室溫下15分鐘，產生淡藍色，加入中止劑(1 M 磷酸)顏色變為黃色，反應3分鐘，測450 nm吸光值，30分鐘內判讀完畢。呈色吸光值與8-OHdG 標準溶液0.5、2、8、20、80和200 ng/mL濃度之log值與吸光值作圖，再以樣本之吸光值換算出濃度，結果以$\mu$g/g creatinine表示。

## 參、結果與討論

### 一、基本人口學資料及改善前環境測定基準值

本研究之研究對象扣除女性以及外勞作業人員後共有55人，包括A鑄造工廠(暴露組)30人、C廠(對照組)25人(如表1)。A廠勞工之年齡為43.63±12.98歲，C廠勞工之年齡為50.68±7.4歲；A廠勞工之工作年資為8.97±7.40年，C廠勞工之之工作年資為10.08±9.58年。故在年齡及工作年資方面，A廠勞工大於C廠勞工，且呈顯著差異。至於BMI、目前抽菸習慣、喝酒習慣、吃檳榔習慣方面，A、C兩工廠並未明顯差異。而在改善前之基準點方面(表2)，A廠環境測定資料顯示，其可呼吸性粉塵濃度為2.87±1.38 mg/m$^3$，可呼吸性結晶型二氧化矽濃度為0.50±0.26 mg/m$^3$。C廠環境測定資料顯示，其可呼吸性粉塵濃度為0.32±0.23mg/m$^3$，可呼吸性結晶型二氧化矽濃度為0.14±0.06 mg/m$^3$。很明顯地，A廠在可呼吸性粉塵及結晶型二氧化矽濃度皆高於C廠，且呈現顯著差異。

**表1　研究對象基本人口學及生活習慣變項分佈**

| 變項 | A廠(30人) | C廠(25人) | P value |
|---|---|---|---|
| 年齡（歲） | 43.63±12.98 | 50.68±7.40 | <0.05 |
| BMI(kg/m$^2$) | 24.90±2.83 | 25.35±3.03 | 0.58 |
| 年資（年） | 8.97±7.40 | 10.08±9.58 | <0.05 |
| 目前抽菸習慣N(%) | | | 0.78 |
| 無 | 13(48.1) | 13(52.0) | |
| 有 | 14(51.9) | 12(48.0) | |
| 喝酒習慣N(%) | | | 0.63 |
| 每月少於一次 | 20(71.4) | 15(65.2) | |
| 一週三次以上 | 8(28.6) | 8(34.8) | |
| 吃檳榔習慣N(%) | | | 0.40 |
| 無 | 18(64.3) | 18(75.0) | |
| 有 | 10(35.7) | 6(25.0) | |

**表2　空氣採樣資料依廠別描述與檢定(基準點)**

| 變項 | A廠 | | C廠 | | P值 |
|---|---|---|---|---|---|
| | 樣本素 | 平均值±標準差 | 樣本素 | 平均值±標準差 | |
| 個人採樣 | | | | | |
| 可呼吸性粉塵濃度(mg/m$^3$) | 8 | 2.87±1.38 | 17 | 0.32±0.23 | <0.05 |
| $SiO_2$ (mg/ m$^3$) | 8 | 0.50±0.26 | 17 | 0.14±0.06 | <0.05 |

在肺功能方面(表3)，若肺活量FVC%＜80%，則屬於限制型(restrictive) 肺功能異常；若肺活量

**表3　肺功能依工廠類別之檢定**

| 分析變項 | A廠(n=30) | | C廠(n=25) | | P value |
|---|---|---|---|---|---|
| | 正常 N(%) | 異常 N(%) | 正常 N(%) | 異常 N(%) | |
| 肺功能 | | | | | |
| 1.肺活量% | 27(90.0) | 3(10.0) | 24(96.0) | 1(4.0) | 0.62 |
| 2.一秒率比值 | 27(90.0) | 3(10.0) | 25(100) | 0 | 0.24 |

FEV1/FVC%＜70%，則屬於阻塞型(obstructive) 肺功能異常。而A廠有10%勞工呈現限制型(restrictive)及阻塞型(obstructive)肺功能異常，C廠有4%勞工呈現限制型(restrictive)肺功能異常；A、C兩工廠並未明顯差異。在控制干擾因子方面，表4列出當在控制抽煙生活習慣、工廠別等因子時，進行肺功能複迴歸模式分析；結果顯示肺功能FVC%、FEV1/FVC%與生活習慣變相並未呈現顯著相關。

勞工尿中8-OHdG/Cr濃度部分(表5)，A廠勞工尿中8-OHdG/creatinine 濃度為7.14±6.76μg/g，C廠勞工尿中8-OHdG/creatinine 濃度為4.27±2.77μg/g。A廠勞工尿中8-OHdG/creatinine 濃度隨著年齡增加而減少，C廠勞工尿中8-OHdG/creatinine 濃度隨著年齡增加而增加，但並未達到顯著相關。而在45歲以下之勞工，其尿中8-OHdG/creatinine 濃度，A廠為10.89±7.70μg/g，B廠為2.55±1.19μg/g，兩者具有顯著差異。而在飲酒方面，C廠勞工有飲酒習慣者，其尿中8-OHdG/creatinine 濃度為5.87±2.80μg/g，不飲酒者，其濃度為3.19±2.41μg/g，兩者具有顯著差異。進行其餘變數之檢定，如BMI、吸菸習慣、吃檳榔習慣、FVC%、FEV1/FVC%，勞工尿中8-OHdG/creatinine 濃度並未明顯差異。

表6列出在控制工廠別、年齡(年資)、抽煙、喝酒、吃檳榔等生活習慣因子後，進行複迴歸模式分析尿中Log(8-OHdG/creatinine)；結果顯示，尿中8-OHdG/creatinine取對數值後和年齡(年資)、吃檳榔習慣呈現顯著相關。Log(8-OHdG/creatinine)濃度隨著年齡(年資)略減，而有吃檳榔習慣者，其尿中Log(8-OHdG/creatinine)增加0.38。

**表4　控制生活習慣因子後肺功能複迴歸模式**

| | 迴歸係數 | 標準誤 | 截距 | P值 |
|---|---|---|---|---|
| 肺活量% | | | | |
| 常數 | 95.96 | 6.20 | 15.49 | <0.05 |
| 廠別 | 3.43 | 2.69 | 1.28 | 0.21 |
| 目前抽菸情況(有/無) | 3.28 | 4.33 | 0.76 | 0.45 |
| 一秒率% | | | | |
| 常數 | 78.21 | 3.36 | 23.31 | <0.05 |
| 廠別 | 0.89 | 1.46 | 0.61 | 0.55 |
| 目前抽菸情況(有/無) | -2.24 | 2.35 | -0.96 | 0.34 |

**表5　兩工廠分層檢定影響尿中8-OHdG/Cr濃度之變數描述(扣除7位極端值)**

| 變　項 | | A廠人(23人) | C廠人(23人) | P value |
|---|---|---|---|---|
| 8-OHdG/Cr μg/g creatinine | | 7.14±6.76 | 4.27±2.77 | 0.58 |
| 年齡(year) | 45歲以 | 10.89±7.70 | 2.55±1.19 | ＜0.05 |
| | 45-52歲 | 4.98±4.82 | 3.06±1.82 | 1.0 |
| | 52歲以上 | 3.25±3.74 | 5.64±3.03 | 0.06 |
| | P value | 0.10 | 0.11 | |
| BMI(kg/m$^2$) | 23以下 | 6.69±6.90 | 2.81±0.25 | 0.64 |
| | 23~26 | 4.79±5.12 | 4.46±3.27 | 0.61 |
| | 26以上 | 9.37±8.19 | 4.24±2.38 | 0.28 |
| | P value | 0.14 | 0.80 | |
| 吸菸習慣 | 吸菸 | 6.99±5.05 | 3.87±2.42 | 0.14 |
| | 不吸菸 | 7.62±9.27 | 4.58±3.08 | 0.55 |
| | P value | 0.49 | 0.58 | |
| 飲酒習慣 | 飲酒 | 8.85±6.32 | 5.87±2.80 | 0.53 |
| | 不飲酒 | 6.57±6.94 | 3.19±2.41 | 0.68 |
| | P value | 0.24 | ＜0.05 | |
| 吃檳榔習慣 | 無 | 0.30±7.42 | 4.78±3.06 | 0.56 |
| | 有 | 8.15±5.74 | 2.77±1.46 | 0.11 |
| | P value | 0.43 | 0.19 | |
| FVC% | 正常 | 6.67±6.82 | 4.01±2.54 | 0.43 |
| | 異常 | 12.08±4.76 | 9.94 | 1.00 |
| | P value | 0.23 | 0.10 | |
| FEV1.0/FVC% | 正常 | 7.58±6.92 | 4.27±2.77 | 0.43 |
| | 異常 | 2.57±1.05 | 0 | 0.23 |
| | P value | 0.51 | - | |

## 二、追蹤工程介入改善後的情形

本研究主要針對高粉塵暴露之作業區，拆模機、集塵設備、廢砂堆放區，進行工程改善；即針對A廠大型鑄件之拆模機，配合起重機行徑動線，規劃具簾幕效果之噴水霧裝置。結果顯示，A、C二廠介入改善前後及追蹤之情形如表7。A鑄造廠在實施作業環境改善前、

**表6　控制生活習慣因子後之尿中Log 8-OHdG/Cr複迴歸模式**

| | 迴歸係數 | 標準誤 | 截距 | P值 |
|---|---|---|---|---|
| 常數 | 1.459 | 0.355 | 4.12 | <0.05 |
| 廠別(A/C) | -0.08 | 0.09 | -0.99 | 0.33 |
| 年齡(年) | -0.02 | 0.01 | -2.697 | <0.05 |
| 目前抽菸情況(有/無) | -0.01 | 0.16 | -0.09 | 0.93 |
| 目前喝酒習慣(有/無) | -0.16 | 0.78 | -0.88 | 0.39 |
| 目前吃檳榔習慣(有/無) | 0.38 | 0.18 | 2.147 | <0.05 |

**表7　兩工廠介入改善前後及追蹤之情形**

| | A廠 | | | C廠 | | |
|---|---|---|---|---|---|---|
| | 改善前檢測 | 改善後追蹤 | P值 | 基準點 | 後續追蹤 | P值 |
| 可呼吸性粉塵濃度($mg/m^3$) | 2.87±1.38 | 1.60±0.70 | 0.07 | 0.32±0.23 | --- | --- |
| $SiO_2$ ($mg/m^3$) | 0.50±0.26 | 0.22±0.11 | <0.05 | 0.14±0.06 | --- | --- |
| 用力肺活量(公升) | 3.69±0.75 | 4.72±0.92 | <0.001 | 3.82±1.00 | 3.82±0.95 | 0.55 |
| 肺活量% | 96.61±14.27 | 123.94±18.42 | <0.001 | 105.30±24.00 | 105.39±22.36 | 0.58 |
| 一秒最大呼氣量(公升) | 3.01±0.72 | 3.88±0.84 | <0.001 | 3.22±0.78 | 3.06±0.72 | 0.07 |
| 一秒率% | 81.12±8.48 | 81.71±6.28 | 0.71 | 84.84±5.75 | 80.34±5.09 | < 0.05 |
| *尿中8- OHdG (ng/ml) | 28.21±38.87 | 14.12±9.67 | 0.37 | 17.78±39.18 | 7.71±6.10 | 0.16 |
| *尿中8- OHdG/Cr μg/g creatinine | 11.51±16.44 | 8.47±4.80 | 0.97 | 4.80±3.52 | 5.43±2.87 | 0.15 |

備註：*進行介入改善前後配對分析者計有A廠22人、 C廠21人；而尿中8- OHdG (ng/ml)與尿中8- OHdG/Cr(μg/g creatinine)個案數，A廠遺失2人，成為20人。

後進行個人採樣，其可呼吸性粉塵濃度($mg/m^3$)分別為2.87±1.38$mg/m^3$、1.60±0.70$mg/m^3$；其可呼吸性結晶型二氧化矽濃度($mg/m^3$)分別為0.50±0.26$mg/m^3$、0.22±0.11$mg/m^3$。介入改善後之環境測定數值已經明顯降低，其可呼吸性結晶型二氧化矽濃度呈現顯著差異；顯示該工程改善已經明顯降低勞工之暴露值。而C廠當作對照組，並未介入工程改善，其環境測定值假設沒有變化，可呼吸性粉塵濃度($mg/m^3$)為0.32±0.23$mg/m^3$；其可呼吸性結晶型二氧化矽濃度($mg/m^3$)為0.14±0.06$mg/m^3$。

在針對A鑄造廠同樣的研究對象進行介入改善前後肺功能指標FVC、FVC%、FEV1檢測，都可以看到肺功能指標在作業環境改善前後有明顯的增加，並且有統計上之顯著意義。FVC(L)自3.69±0.75增至4.72±0.92，FVC%自96.614±14.27增至123.94±18.42，FEV1(L)自3.014±0.72增至3.88±0.84。但是，對於C廠在基準點及後續追蹤，針對同樣研究對象之肺功能改變進行檢定並未發現有顯著的差異(請見表7)；而且FEV1.0/FVC%反而自84.84±5.75降至80.34±5.09。

在A鑄造廠實施作業環境改善前後8-OHdG濃度檢測，不論有無校正尿中creatinine的濃度，都可以看到改善前的氧化壓力高於改善後的氧化壓力，但經配對同樣的研究對象後檢視改善前後之差異，並沒有發現有統計上之顯著意義。其氧化傷害的指標產物隨著現場工程改善而下降，數值自11.51±16.44降至8.47±4.80。將時間變數納入分析，以GEE模式檢視尿中8-OHdG及8-OHdG /creatinine與基準點及追蹤後、工廠別、抽菸習慣、年齡等變項之關係。如表8，在校正A、C鑄造廠、抽菸習慣、年齡等變項後，後續追蹤之尿中8-OHdG比基準點當時之數值低了15.27ng/ml。

**表8　鑄造廠在基準點及追蹤後與8-OHdG/Cr GEE模式分析**

| | 係數. | 標準誤. | 標準差 | P值 | 95%下限信賴區 | 95%上限信賴區 |
|---|---|---|---|---|---|---|
| 8-OHdG(ng/ml) | | | | | | |
| 基準點及追蹤後(後/前) | -15.27 | 6.87 | -2.22 | <0.05 | -28.73 | -1.81 |
| 工廠別(A/C) | 11.77 | 7.40 | 1.59 | 0.11 | -2.73 | 26.27 |
| 抽菸習慣 | 2.52 | 7.24 | 0.35 | 0.73 | -11.66 | 16.70 |
| 年齡 | 0.04 | 0.38 | 0.11 | 0.91 | -0.71 | 0.79 |
| 常數 | 21.05 | 25.50 | 0.83 | 0.41 | -28.93 | 71.03 |
| 8-OHdG/Cr (μg/g creatinine) | | | | | | |
| 基準點及追蹤後(後/前) | -2.17 | 2.13 | -1.02 | 0.31 | -6.35 | 2.00 |
| 工廠別(A/C) | 6.81 | 2.29 | 2.97 | <0.05 | 2.31 | 11.31 |
| 抽菸習慣 | -0.95 | 0.24 | -0.42 | 0.67 | -5.35 | 3.45 |
| 年齡 | 0.10 | 0.12 | 0.84 | 0.40 | -0.13 | 0.33 |
| 常數 | -2.82 | 7.91 | -0.36 | 0.72 | -18.33 | 12.68 |

而在本研究中，經由工程介入後，粉塵濃度亦逐漸下降。而在鑄造業工廠中，各工作製程之工作空間並未以硬體建築物分隔開，為彼此開放空間；故本研究針對重點污染區進行改善，但此效果可影響至整廠之工作勞工。因此雖局部地方改善，但整廠勞工之FVC、FVC(%)、FEV1.0肺功能已經明顯改善；且勞工尿中8-OHdG/creatinine 改善前後雖未達明顯差異，但其濃度已經下降。這些健康改善效應，在對照組C廠並未有如此現象。

再以GEE檢視尿中8-OHdG/creatinine(表8)，發現在校正基準點及追蹤後、抽菸習慣、年齡等變項後，A鑄造廠比C鑄造廠高出6.81μg/g creatinine(CI 2.31~11.31)。將A、C鑄造廠、基準點及追蹤後、抽菸習慣、年齡等變項與FVC%之關係以GEE模式檢視(表9)，在基準點及追蹤後、年齡此兩變項有統計上之顯著意義。也就是後續追蹤之FVC%比起基準點當時之數值高出13.35。因此結論為鑄造廠作業人員其氧化傷害與肺功能有明顯之改變，而這個改變可能與作業環境之改善有關。

## 肆、致謝

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表9　研究個案肺功能GEE模式分析

| 肺功能 | 係數 | 標準誤 | 標準差 | P值 | 95%下限信賴區 | 95%上限信賴區 |
|---|---|---|---|---|---|---|
| 肺活量% | | | | | | |
| 基準點及追蹤後(後/前) | 13.35 | 4.77 | 2.80 | <0.05 | 4.00 | 22.70 |
| 工廠別(A/C) | -0.91 | 5.07 | -0.18 | 0.86 | -10.84 | 9.02 |
| 抽菸習慣 | 2.94 | 4.98 | 0.59 | 0.56 | -6.82 | 12.71 |
| 年齡 | -0.58 | 0.26 | -2.21 | <0.05 | -1.10 | -0.07 |
| 常數 | 115.85 | 17.82 | 6.50 | <0.05 | 80.92 | 150.78 |
| 一秒率% | | | | | | |
| 改善情況(後/前) | -1.85 | 1.43 | -1.29 | 0.20 | -4.65 | 0.96 |
| 工廠別(A/C) | -2.31 | 1.52 | -1.51 | 0.13 | -5.30 | 0.68 |
| 抽菸習慣 | 0.87 | 1.52 | 0.57 | 0.57 | -2.11 | 3.86 |
| 年齡 | -0.14 | 0.08 | -1.74 | 0.08 | -0.30 | 0.02 |
| 常數 | 94.92 | 5.37 | 17.69 | <0.05 | 84.40 | 105.43 |

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# Health risk assessment by measuring plasma malondialdehyde (MDA), urinary 8-hydroxydeoxyguanosine (8-OH-dG) and DNA strand breakage following metal exposure in foundry workers

Hung-Hsin Liu[b], Ming-Hsiu Lin[c], Po-Ching Liu[a], Chia-I Chan[a], Hsiu-Ling Chen[a,*]

[a] Institute of Occupational Safety and Hazard Prevention, Hung Kuang University, 34 Chung Chie Rd., Sha Lu, Taichung 433, Taiwan
[b] School of Occupational Safety and Health, Chung Shan Medical University, Taichung, Taiwan
[c] Institute of Occupational Safety and Health, Council of Labor Affairs, Taipei, Taiwan

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ABSTRACT

Silica particles and metals are important occupational hazards in foundry workers, and exposure may result in DNA damage and lipid peroxidation through oxidative stress. This study aimed to compare oxidative damage by measuring the levels of plasma malondialdehyde (MDA), urinary 8-hydroxydeoxyguanosine (8-OH-dG) and DNA strand breakage in workers at two foundry plants (exposure group) and in town hall employees (control group) in central Taiwan. Air samples for metals analysis in the workplace were also collected to assess the health risk to foundry workers.

Significantly higher MDA levels (4.28 μM versus 1.64 μM), DNA strand breakage (6.63 versus 1.22), and 8-OH-dG levels (5.00 μg/g creatinine versus 1.84 μg/g creatinine) were found in exposure group compared with the control group. Higher levels of these parameters were also found in workers involved in manufacturing than in workers involved in administration. Higher air respirable dust concentrations were found in manufacturing departments (0.99 mg/m³) than in administrative departments (0.34 mg/m³). The health risk assessment on metals exposure showed that the cancer risk for Cd, Cr and Ni were all above $1 \times 10^{-6}$. Future studies are necessary to determine whether metals exposure can contribute to oxidative damage in foundry workers.



## 1. Introduction

Foundry plants have various treatment processes for reclaiming bentonite-bonded molding sands, which consist of silica sand, coal dust and clay, with particle-sizes ranging from 0.1 to 0.4 mm [1]. Two main procedures take place in a foundry: sand molding and metal casting. Sand molding includes core sand and binder, core making and then the casting process which consists basically of pouring liquid metal into a mold containing a socket into the geometry desired for the final part of the process. After casting cooling, shakeout and cleaning, the metals and sand are recovered. The flow chart in Fig. 1 refers to the report by Ribeiro and Filho [2]. The study consisted of 610 workers employed at a foundry where it was found that a total of 846 injuries were recorded on the personnel injuries files. The highest number of injuries involved foreign particles in eyes (40%), strains, pulls and tears (31%), bruises (11%), cuts and puncture wounds (9%), burns and scalds (5%), and broken bones (4%) [3]. In addition, grinders experienced more eye injuries, and molders had more strains, pulls and tears. Particle injuries were obviously more important than any of the other physical injuries recorded in the foundries. Environmental air sampling has shown that chromium species (Cr), iron (Fe) and aluminum (Al) are at high levels in the emission or ambient air outside the foundry in an area between no foundry activity and foundry activity [4,5]. Moreover, a leaching study finds high silver (Ag), arsenic (As), barium (Ba), cadmium (Cd), chromium (Cr), and lead (Pb) in foundry molding sands [6]. Although industrial foundries vary in terms of the type of metal being poured, the sand casting process, the type of furnace (induction, electric arc, and cupola) and finishing process (grinding, blast cleaning, and coating), the basic process and hazards including particles and metals remain the most important occupational hazards in the foundry industry.

Many studies have suggested that silica particles may induce reactive oxygen species (ROS) generation [7–9], which overwhelms antioxidant defenses in the lung and causes lipid peroxidation and cell damage [10]. ROS can also cause many types of DNA damage, including gene mutation, exchange of sister chromosomes

*Abbreviations:* ROS, reactive oxygen species; 8-OH-dG, 8-hydroxydeoxyguanosine; comet, single-cell gel electrophoresis assay; MDA, malondialdehyde; TMOM, the tail moment by Comet assay.

* Corresponding author at: Institute of Occupational Safety and Hazard Prevention, Hung Kuang University, 34 Chung Chie Rd., Sha Lu, Taichung 433, Taiwan. Tel.: +886 4 26318652x4010; fax: +886 4 26319175.
*E-mail address:* hsiulin@sunrise.hk.edu.tw (H.-L. Chen).

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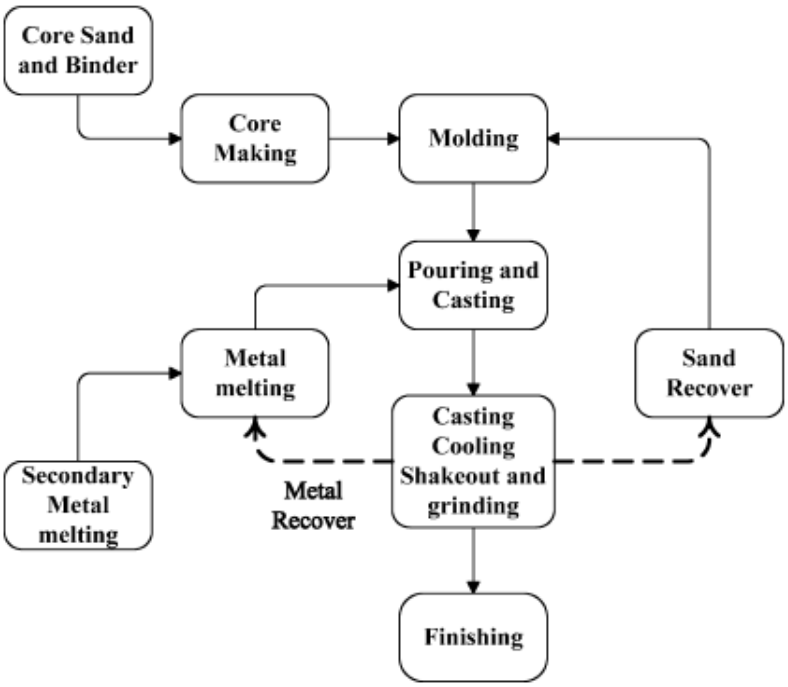


Fig. 1. Operating procedure of the foundry.

and mutagenesis in chromatids [11,12]. Hazardous substances such as metals and other organic compounds can cause an increase in oxidative damage, including malondialdehyde (MDA), 8-hydroxydeoxyguanosine (8-OH-dG), and DNA breakage (single cell gel electrophoresis of comet assay) in workers in the battery plant, cement plant, and metal recovery plants [13–15], and the studies suggest that occupational exposure to incinerators may cause harm via oxidative stress. Meanwhile, exposure to Cr results in the increased production of ROS, lipid peroxidation, and enhances the excretion of urinary lipid metabolites [16], as well as lipid peroxidation and catalase activity elevates in liver, kidney and brain of Pb exposed rats [17–19]. Ni compounds can elicit chromosome aberrations, lung cancer risk [20] and are classified as human carcinogens by the International Agency of Research on Cancer (IARC) [21]. These results suggest that exposure to silica particles and many metals may result in DNA damage and lipid peroxidation through oxidative stress.

Although many studies have indicated neuro-toxic and health effects in foundry workers [22,23], little is known about the status of oxidative stress in workers at occupational smelting factories potentially exposed to more silica particles and metals. Here, we compared the oxidative stress status by measuring the levels of plasma malondialdehyde (MDA), urinary 8-hydroxydeoxyguanosine (8-OH-dG) and DNA strand breakage in workers potentially exposed to hazardous substances, including silica sand and metals at two foundry plants (exposure group) and in town hall employees (control group) in central Taiwan. Air samples for metals analysis in the workplace were also collected to assess the health risk of foundry workers.

## 2. Materials and methods

### 2.1. Subjects

The study was conducted in two typical foundry plants in central Taiwan. Plant A typically uses an induction furnace for metal melting and plant B uses a cupola. A pre-sampling walk-through was conducted to determine the layout of each work site and its borders. In principle, the zones in the foundry plant are based on various operational functions. Areas which included: core making, smelting furnace, molding, sand shakeout, grinding, sand recovery, and administration, were selected for study.

Fifteen and 26 workers were recruited from plant A and B, respectively (exposure group) and 27 administrative staff from the town hall (control group) were also included. Each employee was asked to fill out a questionnaire asking for information about personal characteristics (gender, age, height, weight, residence neighborhood, etc.), life style (e.g., tobacco usage and alcohol intake), and occupational history (e.g., working history at current place of employment, working environment, job titles, periods of employment, and use of protective equipment). Body mass index (BMI, kg/m$^2$; weight in kg divided by the square of the height in meters (m)) was also calculated for each participant. The study was approved by the Ethics Committee of the Kuang Tien General Hospital (Taichung, Taiwan).

### 2.2. Blood collection

The sampling day was Friday, the last working day of the week. The workers completed an overnight fast before blood sampling, and Friday was chosen as it would represent the highest accumulation of hazardous chemicals for the week in this type of environment. Each participant provided 2 mL of venous blood, drawn into chemically clean tubes containing heparin. One milliliter of the blood sample was centrifuged at 1000 × $g$ for 10 min to separate blood cells and plasma. Plasma was stored at −85 °C until analysis of MDA. After cryoprotectants (1:1 ratio) had been added to the other 1 mL of blood, the samples were stored at −85 °C until the comet assay.

### 2.3. Urine collection

Urine samples were collected in polyethylene bottles (which had been washed with 0.2% $HNO_3$) from the first urination in the morn-

**Table 2**
MDA, 8-OH-dG and TMOM of the workers in exposure (foundry plants) and control groups.

| | Exposure ($n$ = 41) | Control ($n$ = 27) | $p$-Value |
|---|---|---|---|
| MDA (μM)[a] | 4.28 ± 2.11 | 1.64 ± 0.81 | <**0.0001**[*] |
| 8-OH-dG (μg/g creatinine)[a] | 5.00 ± 4.92 | 1.84 ± 1.53 | **0.001**[*] |
| TMOM[a,b] | 6.63 ± 3.99 | 1.22 ± 0.76 | <**0.0001**[*] |

[a] Mean ± standard deviation, data are analyzed by Wilcoxon test.
[b] TMOM (tail moment).
[*] $p$-Value < 0.05.

**Table 3**
MDA, 8-OH-dG and TMOM of the workers in manufacturing department and in administrative department.

| Oxidative damage | Departments | |
|---|---|---|
| | Administrative dep. ($n$ = 3) | Manufacturing dep. ($n$ = 38) |
| MDA (μM)[a] | 2.62 ± 0.54 | 4.41 ± 2.13 |
| 8-OH-dG (μg/g creatinine)[a] | 1.61 ± 1.05 | 5.27 ± 5.01 |
| TMOM[a,b] | 4.52 ± 3.19 | 6.80 ± 4.03 |

[a] Mean ± standard deviation.
[b] TMOM (tail moment).

the control group exercised regularly compared with the exposure group.

### 3.2. Oxidative stress markers

We found significantly higher MDA levels in the exposure group compared with the control group (4.28 μM versus 1.64 μM, respectively; $p < 0.0001$), as well as greater DNA strand breakage (6.63 versus 1.22, respectively; $p < 0.0001$). The differences in 8-OH-dG levels between the two groups also showed a similar trend (5.00 μg/g creatinine versus 1.84 μg/g creatinine, respectively; $p < 0.0001$; Table 2).

### 3.3. Working status and oxidative stress markers

All workers were categorized, based on their job titles or work departments, as members of the manufacturing department ($n$ = 38) or administrative department ($n$ = 3) in the two foundry plants. MDA levels, 8-OH-dG levels and DNA strand breakage were significantly higher in manufacturing workers than in administrative workers, regardless of which foundry they belonged to (Table 3).

### 3.4. Environmental monitoring inside the foundry

Forty respirable air samples were collected inside the foundry, and the dust and metal concentrations are shown in Fig. 2. Higher dust concentrations were found in the manufacturing departments (0.99 mg/m$^3$) than in the administrative departments (0.34 mg/m$^3$). Levels of Al, Fe, Mn, Ni, Pb, and Zn were higher in the manufacturing departments than in the administrative departments.

### 3.5. Risk assessment of heavy metals exposure in foundry workers

Cd, Cr and Ni are recognized as human carcinogens or are suspected to be human carcinogens by the IARC. The health risk assessment on metals exposure showed that the cancer risk of Cd ($2.34 \times 10^{-4}$), Cr ($7.92 \times 10^{-3}$) and Ni ($5.76 \times 10^{-5}$) were all above $1 \times 10^{-6}$ (Table 4). Non-cancer risk assessment also showed that the hazard index (HI) was above 1. This means that workers exposed to Cd, Cr, Ni and Mn in foundries are at risk of bronchus cancer, lung cancer and impairment of neurobehavioral function.

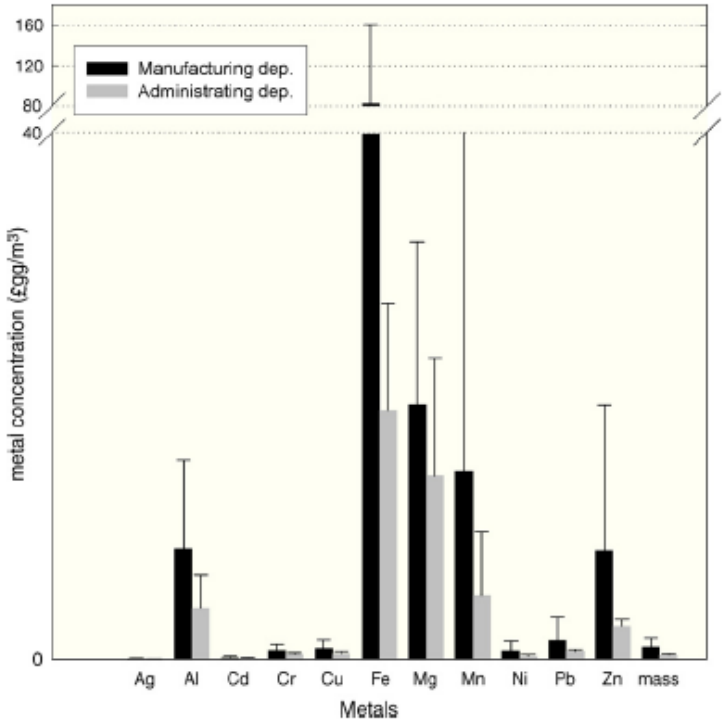


**Fig. 2.** Particle mass (mg/m$^3$) and metal concentration (μg/m$^3$) of respirable particles between manufacturing department and administrating department in the foundry plants (manufacturing department: sample size = 34, administrating department: sample size = 6).

**Table 4**
Health risk assessment for metals in manufacturing departments in foundry.

| | Cd | Cr | Ni | Mn |
|---|---|---|---|---|
| Impairment | Lung, trachea, bronchus cancer [35] | Lung cancer [34] | Lung cancer [33] | Impairment of neurobehavior function [36] |
| Unit risk ($\mu g/m^3$)$^{-1}$ | $1.8 \times 10^{-3}$ | $1.2 \times 10^{-2}$ | $2.4 \times 10^{-4}$ | Group D |
| RfC ($\mu g/m^3$) | – | – | – | $5 \times 10^{-4}$ |
| Air levels ($\mu g/m^3$) | 0.13 | 0.66 | 0.24 | 14.26 |
| Risk of carcinogenesis[a] | $2.34 \times 10^{-4}$ | $7.92 \times 10^{-3}$ | $5.76 \times 10^{-5}$ | – |
| Risk on non-carcinogenesis[b] | – | – | – | 28520 |

[a] Risk on cancer = air levels($\mu g/m^3$) × unit risk ($\mu g/m^3$)$^{-1}$.
[b] Hazard index (HI) = air levels($\mu g/m^3$)/RfC ($\mu g/m^3$).

**Table 5**
Summary presentation of research findings related to metallic profiles in aerosol ($\mu g/m^3$) from various industrial sources.

| Character | Size | Ag | Al | Cd | Cr | Cu | Fe | Mg | Mn | Ni | Pb | Zn | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ferroalloy smelter | $PM_{10}$ | – | – | – | – | – | – | – | 0.80 | – | – | – | [29] |
| Foundry | TSP | – | – | – | – | – | – | – | 5.0–39 | – | – | – | [47] |
| Manganese alloy plant | $PM_{10}$ | – | – | – | – | – | – | – | 301 | – | – | – | [23] |
| Iron and steel industry | TSP | – | 0.59 | – | 0.02 | 0.10 | 1.25 | – | 0.07 | 0.01 | 0.15 | 0.19 | [32] |
| Industrial area | $PM_{2.5}$ | – | 0.07 | – | 0.01 | 0.01 | 0.30 | – | 0.01 | 0.004 | 0.01 | 0.04 | [48] |
| Industrial area | $PM_{2.5}$ | – | 0.33 | – | 0.01 | 0.04 | 0.48 | 0.20 | 0.02 | 0.01 | 0.09 | 0.38 | [46] |
| Industrial complex | $PM_{10}$ | – | – | 0.003 | 0.03 | 0.04 | 1.63 | – | 0.05 | 0.04 | 0.24 | 0.24 | [9] |
| Industrial area | $PM_{10}$ | – | 0.57 | 0.01 | 0.04 | 0.02 | 1.07 | 0.29 | 0.06 | 0.02 | 0.18 | 0.48 | [30] |
| Blast furnace during operation | $PM_{2.5}$ | 0.06 | 17.13 | 0.12 | 0.09 | 0.36 | 40.00 | 25.13 | 0.27 | 0.04 | 1.15 | 31.07 | [31] |
| Manufacturing dep. | $PM_{10}$ | 0.05 | 8.42 | 0.13 | 0.66 | 0.86 | 83.03 | 19.31 | 14.27 | 0.62 | 1.50 | 8.28 | This study |
| Administrating dep. | $PM_{10}$ | 0.03 | 3.88 | 0.10 | 0.40 | 0.44 | 18.89 | 13.92 | 4.85 | 0.24 | 0.59 | 2.53 | This study |

–: No data available.

## 4. Discussion

### 4.1. Metals in foundries

Foundry particles from molding sand are composed of a complex chemical mixture which includes silica [1], Al and Fe [5], Mn [29], Cr and others [2,4], and the leaching procedure also results in high levels of Ag, As, Ba, Cd, Cr and Pb in molding sand [6].

A comparison of the metal concentrations in the present study to previous studies (Table 5), showed that the air metal concentrations were higher in foundry plants than in a ferroalloy smelter [29] and other industrial areas [9,30], regardless of whether the samples were taken from administrative departments or manufacturing departments. This means that administrative departments are not completely separate from manufacturing departments, and that administrative workers also need to be protected in the foundry. By comparing the metal concentrations in the present study to those in a blast furnace during operation [31], the manufacturing departments in the present study showed higher Cr, Cu, Fe, Mn and Ni levels than those in a blast furnace during operation. The metal concentrations in the administrative departments were also significantly higher than those collected in the vicinity of industrial areas [9,30,32]. It may be interpreted from these findings that administrative workers have a higher risk of exposure to metals emitted during the operating process in a foundry. The health risk assessment on metals exposure showed that the risk of Cd, Cr and Ni were all above $1 \times 10^{-6}$, while, non-cancer risk assessment also showed that workers were exposed to predominant metals. However, none of them exceeded the threshold limit values of the metals. Therefore, future studies should follow health outcomes including bronchus and lung impairment [33–35], and disorders of neurobehavioral function in foundry workers [36].

### 4.2. Metal exposure and oxidative damage

The relationship between metal exposure and neuropsychological function [22,37,38], oxidative mechanisms [16], and lung cancer risk [20] are under discussion. Levels of 8-oxo-dG in lymphocyte DNA and markers of oxidative damage to lipids and proteins in plasma are associated with environmental $PM_{2.5}$ exposure [39], and epidemiological evidence suggests that exposure to As and Cr may mediate oxidative stress, apoptosis, and carcinogenesis [40]. Massive DNA damage, along with deregulation of cell homeostasis, leads to malignant diseases [41]. Casado et al. [42] indicated that Pb exposure may cause GSH oxidation to GSSG, which shows that the stress index increases significantly, and that lipid peroxide formation is mediated by a metal-driven Fenton reaction. MDA increases under heavy metal stress, and an increasing amount of MDA represents the formation of free radicals in the test microorganism under heavy metal stress [43]. In an *in vitro* study, Cu significantly raises the MDA level more than Cd, whereas catalase activity is significantly reduced by Cd than by Cu [44]. These results provide evidence that metals treatment or metals exposure can induce oxidative stress, as measured by ROS, oxidative enzyme activities or MDA. In this study, significantly higher lipid peroxidation and DNA damage are observed in foundry workers compare to town hall employees. In addition, the levels of these parameters are higher in workers from manufacturing departments than in those from administrative departments, even though they all work in the same foundry. Compared with our previous study, the MDA levels in foundry workers in this study were higher than 0.58–3.20 μM which was found in workers from a bottom ash recovery plant and from fly ash treatment plants [45], and higher than 1.79–2.54 μM which was found in workers from a Cu smelter and from Zn recovery plants [13]. However, the 8-OH-dG level in this study (5.00 μg/g creatinine) was not different from the level in workers from a bottom ash recovery plant and from fly ash treatment plants [45]. These results suggest that blood MDA level may be a sensitive oxidative marker for exposure to occupational hazards, such as heavy metals.

## 5. Conclusion

The present study demonstrated that workers at foundry plants (exposure group) have significantly higher plasma MDA, DNA damage and 8-OH-dG than town hall employees (control group). Together with air sampling, the data showed that larger quantities of metals were leached from manufacturing departments than administrative departments, indicating that elevated oxida-

tive damage in foundry workers was reasonable. However, it is not negligence that administrative workers in foundries were also likely to be exposed to heavy metals emitted from the foundry operating process. In addition, it remains to be determined whether oxidative damage can be attributed to particular metals and particular levels of metals in foundry plants.

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# Oxidative damage in foundry workers occupationally co-exposed to PAHs and metals

Hung-Hsin Liu [b], Ming-Hsiu Lin [c], Chia-I Chan [a], Hsiu-Ling Chen [a,*]

[a] Department of Industrial Safety & Health, Hung Kuang University, Taichung, Taiwan
[b] School of Occupational Safety and Health, Chung Shan Medical University, Taichung, Taiwan
[c] Institute of Occupational Safety and Health, Council of Labor Affairs, Taipei, Taiwan

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ABSTRACT

Occupational exposure to polycyclic aromatic hydrocarbons (PAHs) has been reported in foundries. A higher risk for DNA damage or oxidative damage lesions was also found in occupationally PAH-exposed groups. The aim of this study was to assess PAH exposure by urinary excretion of 1-hydroxypyrene (1-OHP), a biological exposure marker. Furthermore, we aimed to evaluate the oxidative damage of foundry workers with different job tasks and the association between 1-OHP, metal exposure and oxidative damage in foundry workers exposed to pervasive carcinogens.

A higher concentration of 1-OHP was found in the exposed group (0.322 ± 0.289 μg/g creatinine) relative to the control group (0.178 ± 0.289 μg/g creatinine) ($p < 0.05$). Moreover, higher levels of 1-OHP were found in workers involved in manufacturing processes (0.346 μg/g creatinine) compared to administrative workers (0.018 μg/g creatinine). A positive correlation was identified between levels of 1-OHP and 8-hydroxydeoxyguanosine (8-OH-dG), DNA strand breakage and malondialdehyde (MDA) in all study subjects. However, when foundry workers were considered based on their specific job categories, a similar trend for 1-OHP and three oxidative damage markers was only found for DNA strand breakage, but not for 8-OH-dG or MDA. Other factors such as furnace equipment, PAH types, and job categories may contribute to different PAH emissions. The study also suggested that co-exposure to metal and PAHs, and smoking status in foundry industries may also cause the oxidative damage in foundry workers.



## Introduction

Exposure to high levels of polycyclic aromatic hydrocarbons (PAHs) has been reported in several industries and occupations (Boffetta et al., 1997; Bosetti et al., 2007; El Zanan et al., 2006; Makhniashvili et al., 2006). Special PAHs, such as anthracene, fluorene, naphthalene and phenanthrene, are generated in many foundry sands and have been detected in over 79% of foundry sand wastes (Dungan, 2006, Dungan and Reeves, 2007). A leaching study showed that all spent foundry sands contained PAHs, 30% of which was naphthalene. The PAHs varied in different sands regardless of whether the sand was natural or had been in a chemical binder (Ji et al., 2001). Other than PAHs, major hazards in olivine sands or brass foundries include Ni, Cu, Pb and Zn (Dungan, 2008). Therefore, metal exposure is another occupational hazard in the foundry industry (Caylak et al., 2007; Polizzi et al., 2007).

Previous studies have demonstrated that increased concentrations of PAHs in the air at the workplace could induce the formation of DNA strand breaks in the white blood cells of exposed workers at plants producing fireproof materials and bitumen (Marczynski et al., 2005, 2006; Cavallo et al., 2006; Chao et al., 2008). Moreover, a higher risk for DNA damage or oxidative damage lesions was also found in occupationally PAH-exposed coke-oven workers (Cheng et al., 2005; Chao et al., 2008). These data indicate that PAHs are genotoxic substances. A recent occupational study demonstrated increased risks of lung and bladder cancers associated with PAH-related occupations (Bosetti et al., 2007). An epidemiological study has also found a higher risk of lung and respiratory cancers (relative risk (RR)=1.40, 95% confidence interval (CI): 1.31–1.49) and bladder and urinary cancers (RR=1.29, 95% CI 1.06–1.57) in iron and steel foundry workers (Bosetti et al., 2007). The DNA lesions caused by PAH exposure can be sources of toxicity and increase risks of lung and bladder cancers in PAH-related occupations in foundries.

*Abbreviations:* PAHs, polycyclic aromatic hydrocarbons; 1-OHP, 1-hydroxypyrene; 8-OH-dG, 8-hydroxydeoxyguanosine; comet, single-cell gel electrophoresis assay; MDA, malondialdehyde; TMOM, tail moment

* Corresponding author at: Institute of Occupational Safety and Hazard Prevention, Hung Kuang University, 34 Chung Chie Road, Sha Lu, Taichung 433, Taiwan, ROC. Tel.: +886 4 26318652x4010; fax: +886 4 26319175.
*E-mail address:* hsiulin@sunrise.hk.edu.tw (H.-L. Chen).

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Previous studies have suggested that the urinary excretion of 1-hydroxypyrene (1-OHP) can be used as a biomarker for assessing PAH exposure (Hansen et al., 2004; 2008; Bergamaschi et al., 2005; Cavallo et al., 2006). In PAH-exposed individuals, urinary 1-OHP levels were found to increase during the work day and reach maximum levels 3-9 h after the end of the work day (Bouchard and Viau, 1999). The experimental study showed that for five male volunteers exposed to a PAH mixture for 6 h within a one month at an aluminum plant, the average respiratory retention of pyrene 71 h after the onset of exposure was 61%. The half-life of 1-OHP was 9.8 hours (95% CI 7.9-11.7 h), and a balance of 1-OHP absorption and elimination was achieved at the end of the second day (Brzeźnicki et al., 1997). Franco et al. (2008) also discussed the methodologies for using biomarkers such as 1-OHP, PAH-DNA adducts, cytogenetic markers, frequency of chromosomal aberrations and micronucleus induction for the evaluation of cancer risk. The estimated biological exposure index of 1-OHP in iron foundry workers was 1.2 μmol/mol creatinine. Moreover, excretion of 1-OHP increased DNA strand breakage in a dose-dependent manner. Wu et al. (2003) found that the mean concentration of 1-OHP in topside coke oven workers was 93.5 ± 104.4 (ng/ml ± SD), and that urinary 1-OHP and 8-OH-dG levels reflected occupational exposure to PAHs and oxidative DNA damage. Therefore, 1-OHP was utilized as a biological exposure marker for PAH exposure in this study.

Our previous study has been indentified that administrative workers in foundry industries have higher risk of exposure to metals emitted during the operating process (Liu et al., 2009), and some studies also proved that exposure to As and Cr may mediate oxidative stress, apoptosis, and carcinogenesis (Roméo et al., 2000; Shi et al., 2004).

The aim of this study was to assess PAH exposure and oxidative damage in workers with different job categories at steel foundries with high temperature melting processes and to examine the association between 1-OHP, metal exposureand oxidative damage in foundry workers exposed to pervasive carcinogens.

## Material and methods

### Subjects

The study was conducted in two typical foundries in central Taiwan. Plant A typically uses an induction furnace for melting metal, and plant B uses a cupola. The different tasks at the foundries include core making, furnace smelting, molding, sand shakeout, grinding, sand recovery and administration.

The exposure group consisted of 15 and 26 workers at plant A and B, respectively, and the control group consisted of 27 administrative workers from the town hall. Each employee was asked to fill out a questionnaire asking for information about personal characteristics (e.g., gender, age, height, weight, place of residence), lifestyle (e.g., tobacco use and alcohol intake) and occupational history (e.g., work history at current place of employment, work environment, job titles, periods of employment and use of protective equipment). The study was approved by the Ethics Committee of the Kuang Tien General Hospital (Taichung, Taiwan).

### Blood Collection

The sampling day was Friday, the last working day of the week. The workers fasted overnight before blood sampling, and Friday was chosen because it would represent the highest accumulation of hazardous chemicals after a week. Each participant provided 2 mL of venous blood, drawn into chemically clean tubes containing heparin. One milliliter of the blood sample was centrifuged at 1,000 × g for 10 min to separate blood cells and plasma. Plasma was stored at −85 °C until MDA analysis. After cryoprotectants (1:1 ratio) had been added to the other 1 mL of blood, the samples were stored at –85 °C for the comet assay. 250 μL blood were used for metal analysis.

### Urine Collection

Urine samples were collected in polyethylene bottles (which had been washed with 0.2% $HNO_3$) on Friday. The samples were kept at −85 °C for 8-OH-dG and 1-OHP analysis. The 8-OH-dG assay was completed within one week.

### MDA Analysis

Plasma lipid peroxidation was measured as MDA levels. The MDA assay protocol was recently described (Liu et al., 2009).

### Urine 8-OH-dG Assay

Urinary 8-OH-dG levels were determined using a competitive ELISA immunoassay (Japan Institute for the Control of Aging, Shizuoka, Japan) (Mizushima et al., 2001). Data are presented as quantity of 8-OH-dG per creatinine (μg/g creatinine).

### Blood Comet Assay for DNA Strand Breakage

The comet assay protocol was previously described (Chia et al., 2008). The tail moment (TMOM) is considered one of the best indices of comet formation that can be obtained in computerized analyses (Chuang and Hu, 2004).

### 1-OHP Analysis

All urine samples were analyzed for 1-OHP by high-performance liquid chromatography (HPLC) (Jongeneelen et al., 1987; Tsai et al., 2002; Wu et al., 2003). A 10 ml urine specimen was diluted with 1 N hydrochloric acid and 0.1 M acetate buffer (pH 5.0) to a total volume of 20 ml and adjusted to pH 5.0 with 4 M HCl. This mixture was incubated for 20 h with 25 μl of β-glucoronidase (116, 300 units/ml, SIGMA) at 37 ± 0.5 °C in an electronically controlled rotary shaking bath. A sample purification and enrichment cartridge (Sep-Pak ENVI-18 cartridges, 500 mg/3 mL, Supelco) was used to extract the metabolites. The cartridge was washed with 10 ml of distilled water and 5 ml of methanol, and then directly washed with 4 ml of distilled water. The final elution of 1-OHP fractions was performed in 4 ml of methanol. The eluted fractions were evaporated until dry at 50 °C and passed through a syringe filter (PVDF, 0.22 μm, 13 mm, Millpore) reconstituted with 2 ml of methanol. An HPLC system (Waters 2695) containing of a fluorescence detector (Water 474) was used for quantification. Aliquots (20 μl) of each prepared sample were injected into a 150 × 4.6 mm column (Varian C18-A, USA) and analyzed by HPLC with fluorescence detection. The fluorescence conditions were fixed at an excitation wavelength (λex) of 281 nm and an emission wavelength (λem) of 388 nm. Urinary 1-OHP concentrations were adjusted according to creatinine levels and are expressed as μg/g creatinine.

*Blood Metal Analysis*

Blood were diluted by 0.1% $HNO_3$ and 0.02% Triton X-100 (GR for analysis, Merck) according to Palmer et al. (2006) and Rodrigues et al. (2009). HNO3 were ultrapure analytical reagents (TAMAPURE-AA-100). Inductively coupled plasma mass spectroscopy (ICP-MS, Perkin Elmer Sciex ELAN DRCII) was used to analyze the metal concentration.

*Statistical Methods*

The JMP 5.0 (SAS Institute, Cary, NC, USA) software package was used for data management and statistical analysis. The Wilcoxon rank sum test was performed to evaluate differences in 1-OHP levels between different ages, the exposed and control groups, gender ratios, smoking ratios and other factors. The Spearman correlation was also utilized to analyze the correlation between 1-OHP levels and oxidative damage.

## Results

*1-OHP levels*

Significantly higher concentrations of 1-OHP were found in the exposed group (0.322 ± 0.289 μg/g creatinine) than in the control group (0.178 ± 0.289 μg/g creatinine, $p < 0.05$, Fig. 1). Table 1 shows the levels of 1-OHP associated with demographic characteristics, lifestyles and work histories of the foundry workers. The average concentration of 1-OHP in smokers (0.409 μg/g creatinine) was significantly higher than that in nonsmokers (0.212 μg/g creatinine). Similarly, the average concentration of 1-OHP in alcohol drinkers (0.385 μg/g creatinine) was significantly higher than that in nondrinkers (0.206 μg/g creatinine). In addition, higher concentrations of 1-OHP were found in workers who were older than 46.7 years of age relative to those younger than 46.7 years of age. Higher concentrations of 1-OHP were also found in workers who had worked at the plant over 10 years relative to those who had worked less than 10 years. Finally, higher concentrations of 1-OHP were found in workers of the manufacturing department (0.346 μg/g creatinine) relative to administrative workers (0.018 μg/g creatinine). Interestingly, workers at plant A had slightly higher concentrations of 1-OHP than workers at plant B ($p > 0.05$).

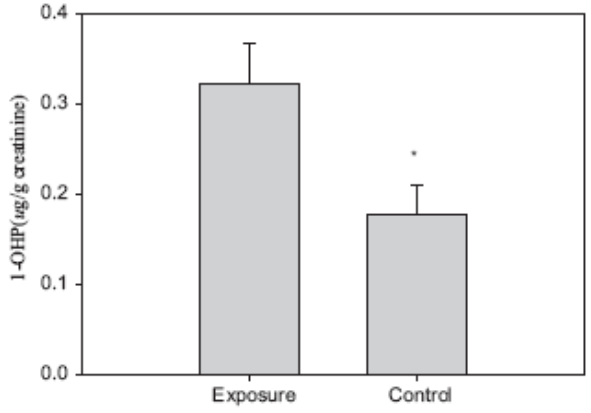


**Fig. 1.** 1-OHP concentrations in PAH-exposed and control groups. Differences in concentrations were analyzed using the Wilcoxon test, and a star indicates that a significant difference was found between the PAH-exposed and control groups.

*1-OHP levels and different job categories*

The highest levels of 1-OHP were found in furnace workers (0.469 μg/g creatinine), followed by maintenance workers (0.392), sand recovery workers (0.350), sand shakeout workers (0.325), coating workers (0.317), painting workers (0.260) and administrative workers (0.018) (Table 2).

*Significantly association between 1-OHP and oxidative damage*

Table 3 shows the Spearman correlations between 1-OHP and oxidative damage in foundry workers and the control group. Significantly positive correlations were found between levels of 1-OHP and levels of MDA, 8-OH-dG and DNA strand breakage in foundry workers and the control group. The concentrations of 1-OHP and oxidative damage in the various departments of the two foundries are shown in Fig. 2. Except for the painting workers,

**Table 1**
Effects of age, working period, smoking status, alcohol intake and working departments on 1-OHP levels in foundry workers.

| Characteristics | n = | 1-OHP (μg/g creatinine)[d] Mean | Standard deviation | P value |
|---|---|---|---|---|
| Foundry | 15 | 0.368 | 0.334 | 0.588 |
| A | 26 | 0.296 | 0.264 | |
| B | | | | |
| Age (years)[a] | | | | 0.331 |
| >46.7 | 23 | 0.367 | 0.348 | |
| ≤46.7 | 18 | 0.265 | 0.185 | |
| Smoking status | | | | **0.043**[c] |
| Yes | 23 | 0.409 | 0.333 | |
| No | 18 | 0.212 | 0.175 | |
| Alcohol intake | | | | **0.048**[c] |
| Yes | 27 | 0.385 | 0.329 | |
| No | 12 | 0.206 | 0.135 | |
| Department | | | | [e] |
| manufacturing | 38 | 0.346 | 0.287 | |
| administrative | 3 | 0.018 | 0.008 | |
| Working period[b] | | | | 0.187 |
| >10 | 20 | 0.369 | 0.285 | |
| ≤10 | 19 | 0.283 | 0.300 | |

[a] : Grouped by mean
[b] : Grouped by median
[c] : $p < 0.05$, data were analyzed by Wilcoxon test
[d] : 1-OHP (μg/g creatinine)
[e] : $n < 10$, the statistical analysis didn't process

**Table 2**
Levels of 1-OHP and oxidative damage in foundry workers in different job categories.

| | N | Mean [a] | Standard deviation |
|---|---|---|---|
| administration | 3 | 0.018 | 0.008 |
| closed-shakeout | 2 | 0.315 | 0.030 |
| Coating | 8 | 0.317 | 0.253 |
| Employer | 2 | 0.238 | 0.298 |
| Furnace | 13 | 0.469 | 0.411 |
| Grinding | 8 | 0.222 | 0.123 |
| maintenance | 1 | 0.392 | – |
| Painting | 1 | 0.260 | – |
| sand recovery | 1 | 0.350 | – |
| shakeout | 2 | 0.325 | 0.128 |

[a] : 1-OHP (μg/g creatinine)

similar trends between levels of 1-OHP and DNA strand breakage were found for different job categories, but the trends between levels of 1-OHP and 8-OH-dG or MDA were not the same when their specific job categories f were considered. Table 4 presents the multivariate regression analysis between 8-OH-dG and interference factors including age, smoking status and urinary 1-OHP or different metal concentrations in blood of the foundry workers. In model 1, the significant positive relationships were found for 8-OH-dG in smokers as compared to nonsmokers (β coefficient=0.370, p=0.040) and for 1-OHP in forth quartile compared to first quartile of all subjects (β coefficient=0.680, p=0.025). In model 2, while PAH and Cd exposure were considered both, the significant positive associations were found between 8-OH-dG levels and Cd exposure (β coefficient=0.619, p=0.041) and for 1-OHP levels in forth quartile compared to first quartile of all subjects (β coefficient = 0.655, p=0.024). Moreover, model 3 showed that the significant higher 8-OH-dG levels was found only for smoking status (β coefficient = 0.374, p=0.036) and for 1-OHP levels (β coefficient = 0.741, p=0.015).

## Discussion

### *PAH exposure in the foundry industry*

PAHs are well-known human carcinogens (Boffetta et al., 1997; Yu, 2002), and are classified as such by the International Agency of Research on Cancer (IARC). Although industrial foundries vary in terms of the type of metal being poured, the sand casting process and the type of furnace and finishing process, the basic manufacturing processes, including melting and pouring at high temperatures, remain the most important occupational hazards in the foundry industry. Therefore, high concentrations of PAHs in ferrous and non-ferrous foundries are potential occupational hazards (Verma et al., 1982; Perera et al., 1994; Makhniashvili et al., 2006).

**Table 3**
Spearman correlation between levels of 1-OHP and oxidative damage in foundry workers and employees of the town city hall.

| | 1-OHP | MDA | 8-OH-dG | TMOM |
|---|---|---|---|---|
| 1-OHP | – | **0.311*** | **0.321*** | **0.392*** |
| MDA | – | – | **0.478*** | **0.341*** |
| 8-OH-dG | – | – | – | 0.156 |

*: $p < 0.05$.

### *Biological exposure markers of PAHs*

Bouchard and Viau (1999) have suggested that levels of 1-OHP in urine increase during the course of a work day, reaching maximum values 3-9 h after the end of the work day. Therefore, in this study, 1-OHP was used as a biological exposure index to assess PAH exposure in foundry workers. The range of 1-OHP concentrations in the foundry workers of this study was 0.011-1.354 μg/g creatinine (0.003-0.651 μmol/ mol creatinine), which was 1.5- to 2-fold higher than that of the control group, which was considered an unexposed group. The data indicate that the foundry workers may potentially be exposed to PAHs. The 1-OHP levels in the foundry workers of the present study were higher than those of the foundry workers in another study (Omland et al., 1994) and equal to the levels of workers exposed to bitumen fumes (Marczynski et al., 2007) and foundry workers of another study (Sherson et al., 1992). In contrast, the levels of 1-OHP in this study were lower than those of temple labors (Kuo et al., 2008), silicon workers (Marie et al., 2009) and some other foundry workers (Bouchard and Viau, 1999) (Table 5).

### *PAH exposure by job category*

In this study, the highest levels of 1-OHP were found in furnace and sand treatment workers. This result is inconsistent with that of Bergamaschi et al. (2005), which indicated that 1-OHP levels were significantly higher in non-smoking workers continuously in the casting process department of the foundry relative to those in the maintenance and furnace areas. Moreover, this result also contrasts with that of Makhniashvili et al. (2006), which suggested that foundry workers exposed to PAHs, especially for those who caster molds and cast strikers, had higher levels of 1-OHP. Therefore, workers may be exposed to PAHs emitted from the furnace and pouring areas of a large foundry does not have well-separated working departments. Furnace type, melting temperature and casting conditions may also affect PAH exposure when working in different departments.

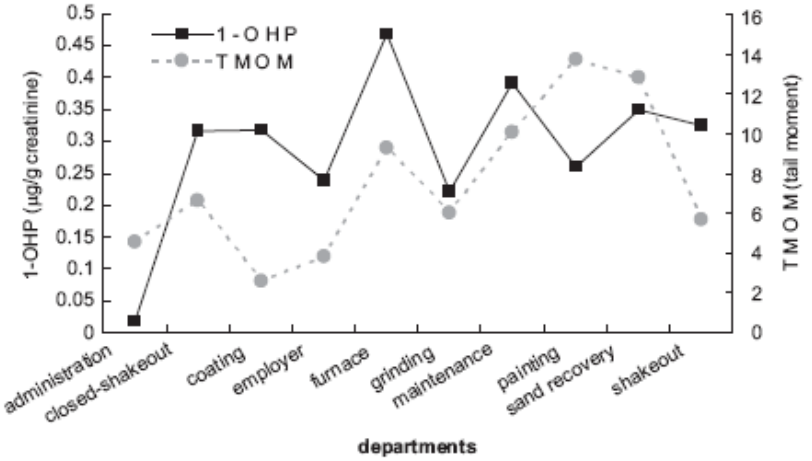


**Fig. 2.** Levels of 1-OHP and DNA strand breakage in different job categories.

**Table 4**
Multivariate regression analysis between 8-OH-dG and interference factors includingage, and smoking status and urinary 1-OHP or blood metal concentrations of the foundry workers.

| Dependent variable | Independent variables | R-square | Regression coefficient | P value |
|---|---|---|---|---|
| Model 1: 8-OH-dG[a] | | 0.169 | | 0.040* |
| | Age | | 0.008 | 0.609 |
| | Smoking status[b] | | 0.370 | 0.040* |
| | 1-OHP(Q2)[c] | | −0.284 | 0.339 |
| | 1-OHP(Q3)[c] | | −0.187 | 0.502 |
| | 1-OHP(Q4)[c] | | 0.680 | 0.025* |
| Model 2:8-OH-dG[a] | | 0.245 | | 0.014* |
| | Age | | 0.011 | 0.517 |
| | Smoking status[b] | | 0.331 | 0.055 |
| | 1-OHP(Q2)[c] | | −0.228 | 0.423 |
| | 1-OHP(Q3)[c] | | −0.163 | 0.539 |
| | 1-OHP(Q4)[c] | | 0.655 | 0.024* |
| | Cd[a] | | 0.619 | 0.041* |
| Model 3: | | 0.196 | | 0.034* |
| 8-OH-dG[a] | Age | | 0.004 | 0.835 |
| | Smoking status[b] | | 0.374 | 0.036* |
| | 1-OHP(Q2)[c] | | −0.331 | 0.262 |
| | 1-OHP(Q3)[c] | | −0.151 | 0.584 |
| | 1-OHP(Q4)[c] | | 0.741 | 0.015* |
| | Crd[a] | | −2.453 | 0.152 |

[a] The data has been logarithmic transformed
[b] The data compared to nonsmoker
[c] The data compare to Q1(Q1: 1-OHP < 0.099; Q2: 0.099≦1-OHP < 0.2779; Q3: 0.2779≦1-OHP < 0.4081; Q4: 1-OHP≧0.4081 μg/g creatinine)

**Table 5**
1-OHP concentrations in different PAH-related occupations.

| References | Subjects (sample size) | 1-OHP concentration |
|---|---|---|
| Our study, 2009 | Foundry workers (41) | 0.322 μg/g creat. (0.011-1.354 μg/g creat.) |
| Omland et al., 1994 | Foundry workers (70) | 0.022-0.027 μmol/mol creat. |
| Sherson et al., 1992 | Foundry workers (45) | 0.70 μmol/mol creat., 95% CI: 0.07-1.47 |
| Marczynski et al., 2007 | Pre-shift bitumen workers (202) | |
| | Post-shift bitumen workers (202) | 0.201 μg/g creat. |
| | | 0.353 μg/g creat. |
| Kuo et al., 2008 | Pre-shift temple labor (95) | 1.20 μg/g creat. |
| | Post-shift temple labor (95) | 1.61 μg/g creat. |
| Marie et al., 2009 | Post-work silicon workers (68) | 0.07-7.9 μmol/mol creat. |
| | | Median: 0.5 μmol/mol creat. |

Note: μg/g creat.=μg/g creatinine

### *PAH exposure and oxidative damage*

*In vivo* studies have shown that PAH exposure can cause formation of DNA adducts (Savela et al., 1996). A nested case control study found that foundry workers with high exposure to crystalline silica, PAHs and various other carcinogenic chemicals had a two-fold higher risk of DNA adduct formation (Rodriguez et al., 2000). A molecular epidemiology study also showed that even foundry workers with relatively low levels of exposure to PAHs ( $< 0.05\ \mu g/m^3$) had increased amounts of DNA adducts relative to control subjects (Perera et al., 1988). Furthermore, PAH-DNA and aromatic-DNA levels and hypoxanthine guanine phosphoribosyl transferase mutation frequencies were increased in workers exposed to B[a]P during a three-year period (60 $ng/m^3$ during the first year, 40 $ng/m^3$ the second year and 36 $ng/m^3$ the third year;) (Perera et al., 1994). Therefore, DNA adducts were found in foundry workers even though they were exposed to low levels of PAHs (Sherson et al., 1992; Perera et al., 1994). In this study, positive correlations were found between urine 1-OHP levels and DNA strand breakage, MDA and 8-OH-dG. These results are consistent to those reported previously that demonstrated that urinary 1-OHP levels were a significant predictor for urinary 8-OHdG levels (Chuang et al., 2002; Pan et al., 2008). Marczynski et al. (2009) also found that levels of 8-oxo-dG and DNA strand breaks were higher in graphite-electrode production workers relative to controls. In contrast, PAH-induced oxidative DNA damage could not be identified in coke oven workers (Zhang et al., 2003), and no correlation was detected between 1-OHP levels and oxidative DNA and RNA lesions in silicon workers. Furthermore, urinary 8-OH-dG was recently suggested to not be a relevant biomarkers of genotoxic PAH exposure (Marie et al., 2009). However, the unstable association between DNA damage and PAH exposure may be affected by different types of PAHs, and co-exposure to other carcinogens such as metal and silica dust in foundry industries may contribute to an individual's level of genotoxic PAHs (Rodriguez et al., 2000; Liu et al., 2009). Therefore, the further analysis assessing the co-exposure of PAHs and metals on oxidative damage were processed and those found the PAHs and Cd indeed causes the elevating of oxidative damage as Roméo et al. (2000) identified.

## Conclusion

The results of this study indicate that high 1-OHP levels are associated with PAH-exposed foundry workers, especially those who work with the furnace, pouring at high temperatures and sand treatment. In summary, we have demonstrated positive correlations between biomarkers of PAHs and DNA strand breakage, MDA and 8-OH-dG. This finding is consistent with previous results, especially regarding levels of DNA strand breakage while the job category has been considered. Meanwhile, co-exposure of PAH and Cd also contributed to elevate 8-OH-dG levels. These results indicate health risk as high levels of DNA damage may increase susceptibility to carcinogenesis and cancer. However, for assessing the potential health effects of the foundry workers, the co-exposure of metal and silica dust and to lay aside the habit of smoking should be considered seriously in future studies.

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# Risk assessment of gaseous/particulate phase PAH exposure in foundry industry

Hung-Hsin Liu[b], Hsi-Hsien Yang[c], Choa-Da Chou[a], Ming-Hsiu Lin[d], Hsiu-Ling Chen[a,*]

[a] Department of Safety, Health and Environmental Engineering, Hung Kuang University, 34 Chung Chie Rd., Sha Lu, Taichung 433, Taiwan
[b] School of Occupational Safety and Health, Chung Shan Medical University, Taichung, Taiwan
[c] Department of Environmental Engineering and Management, Chaoyang University of Technology, Taichung, Taiwan
[d] Institute of Occupational Safety and Health, Council of Labor Affairs, Taipei, Taiwan

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ABSTRACT

Thirty-seven air samplings in different working areas of two foundry industries were collected to assess polycyclic aromatic hydrocarbon (PAH) levels. The average PAH level inside Foundry A was 19.56 μg/m³, which was higher than that in Foundry B (8.26 μg/m³), whereas for the benzo[a]pyrene toxic equivalent (BaPeq) level (38.81 ng/m³ vs. 46.52 ng/m³). A higher PAH level was found for big moulding process than for the small one, and the chemical binder in the different size moulds was hypothesized to be the main cause. The higher PAH levels were found in the painting area (95.51 μg/m³), pouring area (18.42 μg/m³), and inside the office (16.48 μg/m³); as well as the higher BaPeq level was in the painting area (152.3 ng/m³), and the furnace for melting iron (96.9 ng/m³). The gas phase (over 90%) was the major contributor of total PAHs in the manufacturing areas. Moreover, health risk assessment of PAHs exposure showed that lung cancer risks were $9.06 \times 10^{-4}$ and $1.09 \times 10^{-3}$ in Foundries A and B, respectively. This study suggests that the workers shall use appropriate respiratory masks in painting, melting, and pouring areas to prevent their occupational exposure to PAHs.



## 1. Introduction

Several studies have reported that foundry workers may by exposed to high levels of polycyclic aromatic hydrocarbons (PAHs) [1–3]. Special PAHs, such as anthracene (Ant), fluorene (Flu), naphthalene (Nap) and phenanthrene (PA), are generated in many foundry sands and have been detected in over 79% of foundry sand waste [4]. In previous studies, PAH exposure was demonstrated to induce DNA strand breaks in workers exposed to fireproof materials and bitumen [5,6]. Higher risks for DNA damage or oxidative damage lesions have also been found in coke-oven workers with occupational PAH exposure [6,7]. Meanwhile, the increased risks of lung, bladder and urinary cancers were also associated with PAH-related occupations [8,9], as well as the increased risk of cardiovascular disease in foundry workers has also been documented [10]. Therefore, PAH exposure is definitely a cause of many adverse health effects in workers with this kind of exposure.

More than 600 PAHs have been identified; the simplest and most volatile compound is Nap, which has two aromatic rings and is present specifically in the gaseous phase. Meanwhile, Nap has been considered as a potential surrogate for workers with occupational PAH exposure [3]. The PAHs with the most aromatic rings (five- and six-ring) are predominantly in the particulate phase, and the three- and four-ring PAHs exist both in the gaseous and particulate phases, depending on the specific compound and the environmental conditions [11]. The carcinogenic PAHs are five- and six-ring ones, however, a "previous study" reports that the total PAH load of the individual fractions increases steadily with increasing particle size. The inhalable fine particle comprises 31.4% of the total dust and contains 49.9% of the total adsorbed PAH. The percentage of the gaseous phase PAH amounts to 77% of the total PAH load in an iron foundry. Meanwhile, the gas phase contains on average threefold more carcinogenic four- and five-ring PAHs than the particulate phase [12]. A study from Omland et al. [13] in iron foundry workers shows that the average concentration of 16 PAHs is 10.40 μg/m³ in the breathing zone, and the average dust-adsorbed PAH concentration is only 0.15 μg/m³, which demonstrates that the most predominant PAHs are in the gaseous phase. Shimmo et al. [14] indicate that the proportion of gaseous PAHs range from 0% to 100% for each PAH. It is well known that inhalation and skin uptake are both important routes for PAH exposure. Tsapakis and Stephanou [15] suggest that a shift in the gaseous/particulate distribution of PAHs may be caused by a change in the ambient temperature. Meanwhile, high temperatures are found in all manufacturing

*Abbreviations:* PAHs, polycyclic aromatic hydrocarbons; BaPeq, benzo[a]pyrene toxic equivalent; Nap, naphthalene; AcPy, acenaphthylene; Acp, acenaphthene; Flu, fluorene; PA, phenanthrene; Ant, anthracene; FL, fluoranthene; Pyr, pyrene; BaA, benzo[a]anthracene; CHR, chrysene; BbF, benzo[b]fluoranthene; BkF, benzo[k]fluoranthene; BaP, benzo[a]pyrene; IND, indeno[1,2,3,-c,d]pyrene; DBA, dibenz[a,h]anthracene; BghiP, benzo[g,h,i]perylene.

* Corresponding author. Tel.: +886 4 26318652x4010; fax: +886 4 26319175.
*E-mail address:* hsiulin@sunrise.hk.edu.tw (H.-L. Chen).

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processes, especially for metal melting and metal liquid pouring processes. The toxicity of each PAH is related to its ring number, which can affect whether the homologues are in a particulate or gaseous phase. Additionally, because of the high temperature in the foundry environment, it is difficult for the foundry workers to wear masks during their workday. Thus, the distribution of PAH levels in gaseous/particulate phase is important for evaluating the prevention strategy of occupational PAH exposure.

To date, previous studies have used various strategies to present the amount of PAH exposure: 20 PAHs in the Knecht et al. report [12], 16 PAHs in Omland et al. report [13], and 32 PAHs in the spent sand study [16]. In the leaching study of the spent foundry sand, the spent sand is shown to have higher PAH concentration in the green sand than the chemical binder sands, despite the fact that phenolic/ester sands have higher levels of PAHs than furan/acid and silicate sands [16]. These data indicate that PAH concentrations also vary due to the types of foundry sands.

Therefore, this study aims to investigate the gaseous/particulate phase PAHs in two kinds of iron foundry industries in different casting processes. Meanwhile, air samples for PAH analysis in the workplace are also utilized to assess the health risk of PAH exposure for foundry workers.

## 2. Materials and methods

### 2.1. Sampling selection in foundry plants

The study was conducted in two typical foundry plants in central Taiwan. Foundry A typically uses an induction furnace for melting metal, and Foundry B uses a cupola. A pre-sampling walk-through was conducted to determine the layout of each work site and its borders. In principle, the zones in the foundry plant are based on various operational functions. Several areas inside the foundries, including core making, melting furnace, moulding, sand shakeout, grinding, sand recovery, and office areas, as well as areas outside of the foundries were selected for this study. Totally, 37 air samples were taken inside the foundry industries and 6 air samples were taken in office and in outdoor of the 2 industries.

### 2.2. Ambient samples

Airborne samples were collected using a glass cartridge linked to personal air pump samplers (Gillian) with a flow rate of approximately 3 L/min, which was modified by Li et al. report [25]. A glass cartridge containing a glass fibre filter to collect particulate PAHs and total suspended particles in the upper layer and a 5-cm polyurethane foam (PUF) was plugged into the cartridge as the second layer after the filter. XAD-16 resin (1.5 g) and 3-cm PUF were also plugged into the cartridge as the second and bottom layer, respectively, to collect gaseous PAHs. The glass fibre filters were conditioned in the same temperature and humidity. In addition, the filters were weighed 48 h post-conditioning. The post-sampling weights were subtracted from the pre-sampling weights to provide the particle mass in the ambient sampling. Before sampling, the stuffed glass cartridges were cleaned with Soxhlet extracted with a 1:1 solution (Merck) of n-hexane and dichloromethane (v/v) for 24 h, and the cartridges were then dried in an oven at 60 °C to remove residual solvent. During sample transportation, sampling and storage, the glass cartridges were covered with aluminium foil to avoid photolysis degradation.

### 2.3. PAH analysis

The glass fibre filters and cartridges were extracted with Soxhlet with a mixed solvent for 24 h after the ambient sampling was completed. The extracts were then concentrated on a rotary evaporator to 3–5 mL, which was modified by Fang et al. [17]. The subsequent proceeding was the removal of any pollutants to avoid contaminating the gas chromatograph (GC) column. Following the re-concentration procedure, 1.5 mL of extract was obtained after ultra-pure nitrogen treatment. All sampling solvents were analysed using a GC (Agilent 6890)/mass selective (MS) detector (Agilent 5973) equipped with a GC capillary column (Agilent Ultra 2–50 m × 0.32 mm × 0.17 mm) and an automatic sample (Agilent 7683r). The injection volume was 1 μL. A computer workstation was used for the PAH analysis. The temperatures for the injector, transfer line, ion source and Quadruple were 310 °C, 290 °C, 230 °C and 230 °C, respectively. The oven temperature gradient began at 50 °C and rose to 100 °C at a rate of 20 °C/min and then rose from 100 °C to 290 °C at a rate of 3 °C/min; the final temperature of 290 °C was held for 40 min.

In this study, a total of 16 PAH species were analysed, including naphthalene (Nap), acenaphthylene (AcPy), acenaphthene (Acp), fluorene (Flu), phenanthrene (PA), anthracene (Ant), fluoranthene (FL), pyrene (Pyr), benzo[a]anthracene (BaA), chrysene (CHR), benzo[b]fluoranthene (BbF), benzo[k]fluoranthene (BkF), benzo[a]pyrene (BaP), indeno[l,2,3,-c,d]pyrene (IND), dibenz[a,h]anthracene (DBA) and benzo[g,h,i]perylene (BghiP).

### 2.4. Quality control

After consecutive sampling for 8 h, the filters and glass cartridges were stored at −20 °C. The masses of the molecular and fragment ions of PAHs were determined by using the scan mode for pure 16 PAH standards (2000 μg/mL; SUPELCO 48905-U). Qualification of the PAHs was performed by using the selected ion monitoring (SIM) mode. The instruments were calculated using at least five standard concentrations. The correlation coefficient of the calibration curve was >0.995 for a linear least-squares fit of the data. The detection limit was determined from a selected concentration that was slightly lower than the lowest concentration of the calibration curve. Measurements at this concentration were repeated seven times to estimate the standard deviation. The detection limit was determined to be three times of the standard deviation. The detection limit of the GC/MS for the 16 PAHs was between 0.024 ng and 0.740 ng. In this study, recovery efficiency tests for PAHs were accomplished by performing the same sample analysis procedure by adding the standard solution before extraction. The recovery efficiency of particulate PAHs ranged from 79.5% to 99.6% (average 89.1%), and gaseous PAHs ranged from 80.2% to 99.5% (average 89.6%) [18].

### 2.5. Data analysis

The JMP 5.0 (SAS Institute, Cary, NC, USA) and SigmaPlot software (version 8.0, SPSS Inc.) packages were used for data management and statistical analysis. The Wilcoxon rank sum test was carried out to evaluate differences in particle levels between Foundries A and B. Many researchers have calculated the cancer risk of PAH exposure based on the toxic equivalency factors (TEFs), which is considered to be BaPeq [17,19,20], because of BaPeq is a better indicator than total PAH level on characterizing the carcinogenic potency of PAHs. The cancer risks herein were calculated as described by Nisbet and LaGoy [19]. To assess workers' excessive lung cancer risks associated with a 25-year occupational exposure, the unit risk of $7 \times 10^{-5}$ $(\text{BaPeq ng m}^{-3})^{-1}$.

## 3. Results

### 3.1. PAH levels in two foundries

The average particle levels in Foundries A and B were 1.64 $\text{mg/m}^3$ (standard deviation, 1.57) and 1.87 $\text{mg/m}^3$ (standard

deviation, 2.20), respectively (data not shown). The levels were almost equal in the two foundries. The particle measurements in different areas showed that the highest level was found in shakeout area (5.64 mg/m$^3$), the second highest level was in grinding area (3.77 mg/m$^3$), and the third highest level in moulding area (2.93 mg/m$^3$), whereas the lowest one was in outdoor (0.08 mg/m$^3$), and in the office (0.11 mg/m$^3$), respectively. Overall, the particle level inside the foundry plants was significantly higher than those outside of the plants and those of the indoor or outdoor offices (Fig. 1).

The average PAH level inside Foundry A was 19.56 μg/m$^3$, which was higher than in Foundry B (8.26 μg/m$^3$). When we looked at the gaseous/particulate phase PAHs, the gaseous PAH level was 19.3 μg/m$^3$ in Foundry A and 7.98 μg/m$^3$ in Foundry B; however, no statistical difference was found ($p$ value = 0.446). Additionally, the average particulate phase of PAH levels was not significantly different between the two foundries. Meanwhile, the gaseous/particulate phase PAHs was 98.67% and 96.38% in Foundries A and B, respectively. The difference may be due to two- and three-ring PAHs, including AcPy, Acp, Flu, PA, Ant, and Fl (Table 1). The BaPeq level inside Foundry A was 38.81 ng/m$^3$, that was smaller than that in Foundry B (46.52 ng/m$^3$) (Table 2); the reverse trend was found for

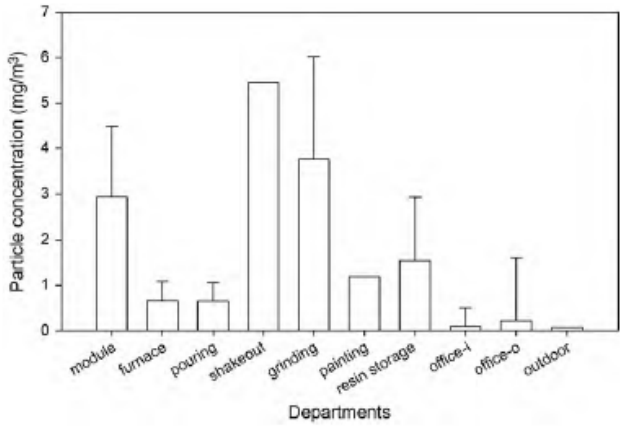


**Fig. 1.** Average particulate concentrations in different working areas of two foundry industries.

**Table 1**
Average concentrations of 16 gaseous and particulate PAHs in two foundry industries.

| PAHs (μg/m$^3$) | Industry A ($n$ = 20) | | | | Industry B ($n$ = 17) | | | |
|---|---|---|---|---|---|---|---|---|
| | Particle | Gas | Total | Gas% | Particle | Gas | Total | Gas% |
| Nap | 0.11 (0.28) | 17.87 (35.06) | 17.98 (35.08) | 99.39 | 0.16 (0.32) | 6.15 (5.94) | 6.31 (5.51) | 97.46 |
| AcPy | N.D. | 0.47 (0.74) | 0.47 (0.74) | 100.00 | 0.02 (0.04) | 0.39 (0.51) | 0.42 (0.50) | 92.86 |
| Acp | N.D. | 0.09 (0.10) | 0.09 (0.10) | 100.00 | N.D. | 0.05 (0.08) | 0.05 (0.08) | 100.00 |
| Flu | N.D. | 0.21 (0.39) | 0.21 (0.39) | 100.00 | 0.01 (0.03) | 0.28 (0.40) | 0.29 (0.40) | 96.55 |
| PA | 0.04 (0.04) | 0.37 (0.55) | 0.41 (0.57) | 90.24 | 0.03 (0.07) | 0.75 (1.74) | 0.78 (1.75) | 96.15 |
| Ant | 0.01 (0.02) | 0.12 (0.25) | 0.13 (0.25) | 92.31 | 0.02 (0.02) | 0.07 (0.11) | 0.09 (0.10) | 77.78 |
| FL | 0.01 (0.02) | 0.11 (0.13) | 0.12 (0.13) | 91.67 | 0.00 (0.01) | 0.20 (0.39) | 0.21 (0.40) | 95.24 |
| Pyr | 0.01 (0.01) | 0.06 (0.10) | 0.07 (0.10) | 85.71 | N.D. | 0.02 (0.02) | 0.02 (0.02) | 100.00 |
| BaA | 0.01 (0.01) | N.D. | 0.01 (0.01) | – | 0.01 (0.02) | 0.01 (0.04) | 0.03 (0.04) | 33.33 |
| CHR | 0.01 (0.01) | N.D. | 0.01 (0.02) | – | N.D. | N.D. | N.D. | – |
| BbF | 0.01 (0.01) | N.D. | 0.01 (0.01) | – | N.D. | N.D. | 0.01 (0.01) | – |
| BkF | 0.01 (0.01) | N.D. | 0.01 (0.01) | – | N.D. | N.D. | N.D. | – |
| BaP | N.D. | N.D. | N.D. | – | 0.02 (0.05) | 0.01 (0.03) | 0.03 (0.06) | 33.33 |
| IND | 0.01 (0.01) | N.D. | 0.01 (0.01) | – | N.D. | 0.03 (0.05) | 0.03 (0.05) | 100.00 |
| DBA | 0.01 (0.01) | N.D. | 0.01 (0.02) | – | N.D. | N.D. | N.D. | – |
| Bghip | 0.02 (0.02) | N.D. | 0.02 (0.02) | – | N.D. | 0.01 (0.01) | 0.01 (0.01) | 100.00 |
| Total | 0.26 (0.26) | 19.30 (35.62) | 19.56 (35.64) | 98.67 | 0.30 (0.41) | 7.98 (7.60) | 8.28 (7.67) | 96.38 |

*Note*: The standard deviation are shown inside parenthesis; N.D.: non-detected; –: it cannot be calculated.

**Table 2**
Average BaPeq concentrations of 16 gaseous and particulate PAHs in two foundry industries.

| BaPeq (ng/m$^3$) | Industry A ($n$ = 20) | | | | Industry B ($n$ = 17) | | | |
|---|---|---|---|---|---|---|---|---|
| | Particle | Gas | Total | Gas% | Particle | Gas | Total | Gas% |
| Nap | 0.11 (0.28) | 17.87 (35.06) | 17.98 (35.8) | 99.39 | 0.16 (0.32) | 6.15 (5.49) | 6.31 (5.51) | 97.46 |
| AcPy | N.D. | 0.47 (0.74) | 0.47 (0.74) | 100.00 | 0.02 (0.04) | 0.39 (0.51) | 0.42 (0.50) | 92.86 |
| Acp | N.D. | 0.09 (0.10) | 0.09 (0.10) | 100.00 | 0.00 (0.01) | 0.05 (0.08) | 0.05 (0.08) | 100.00 |
| Flu | N.D. | 0.21 (0.39) | 0.21 (0.39) | 100.00 | 0.01 (0.03) | 0.28 (0.40) | 0.29 (0.40) | 96.55 |
| PA | 0.04 (0.04) | 0.37 (0.55) | 0.41 (0.57) | 90.24 | 0.03 (0.07) | 0.75 (1.74) | 0.78 (1.75) | 96.15 |
| Ant | 0.07 (0.18) | 1.20 (2.50) | 1.26 (2.49) | 95.24 | 0.23 (0.23) | 0.67 (1.09) | 0.90 (1.01) | 74.44 |
| FL | 0.01 (0.02) | 0.11 (0.13) | 0.12 (0.13) | 91.67 | 0.00 (0.01) | 0.20 (0.39) | 0.21 (0.40) | 95.24 |
| Pyr | 0.01 (0.01) | 0.06 (0.10) | 0.07 (0.10) | 85.71 | 0.00 (0.00) | 0.02 (0.02) | 0.02 (0.02) | 100.00 |
| BaA | 0.52 (0.65) | 0.24 (0.64) | 0.76 (1.15) | 31.58 | 1.20 (1.60) | 1.44 (3.67) | 2.64 (4.27) | 54.55 |
| CHR | 0.09 (0.08) | 0.04 (0.09) | 0.14 (0.16) | 28.57 | 0.00 (0.01) | 0.03 (0.04) | 0.03 (0.04) | 100.00 |
| BbF | 1.26 (1.47) | 0.08 (0.11) | 1.34 (1.42) | 5.97 | 0.11 (0.14) | 0.39 (0.94) | 0.50 (1.00) | 78.00 |
| BkF | 0.62 (0.69) | 0.06 (0.26) | 0.68 (0.83) | 8.82 | 0.15 (0.17) | 0.07 (0.11) | 0.22 (0.25) | 31.82 |
| BaP | 3.73 (4.94) | 0.02 (0.01) | 3.76 (4.94) | 0.53 | 17.84 (54.99) | 10.70 (28.23) | 28.55 (59.11) | 37.48 |
| IND | 1.24 (1.40) | 0.01 (0.02) | 1.25 (1.40) | 0.80 | 0.14 (0.23) | 2.97 (5.29) | 3.11 (5.26) | 95.50 |
| DBA | 9.86 (17.77) | 0.24 (0.55) | 10.10 (17.74) | 2.38 | 1.25 (4.65) | 1.13 (2.40) | 2.39 (6.87) | 47.28 |
| Bghip | 0.17 (0.24) | 0.01 (0.02) | 0.18 (0.23) | 5.56 | 0.04 (0.05) | 0.06 (0.07) | 0.10 (0.10) | 60.00 |
| Total | 17.74 (23.15) | 21.07 (36.9) | 38.81 (43.78) | 54.29 | 21.22 (55.17) | 25.31 (41.88) | 46.52 (67.57) | 54.41 |

*Note*: The standard deviation is shown inside parenthesis; N.D.: non-detected.

**Table 3**
Mean concentrations ($\mu g/m^3$) and BaPeq levels ($ng/m^3$) of 16 gaseous and particulate PAHs by large or small moulds in two foundry industries.

| Departments | N | PAHs | | | | TEQ-PAHs | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Particle | Gas | Total | Gas% | Particle | Gas | Total | Gas% |
| A | | | | | | | | | |
| Big | | | | | | | | | |
| Moulding | 3 | 0.17 (0.05–0.18) | 7.19 (4.09–12.37) | 7.36 (4.27–12.53) | 97.69 | 20.44 (16.84–27.23) | 7.74 (4.30–13.34) | 28.18 (21.56–32.80) | 27.47 |
| Pouring | 2 | 0.68 (0.19–1.17) | 36.88 (9.18–64.57) | 37.56 (9.37–65.74) | 98.19 | 25.94 (17.58–34.31) | 44.13 (10.41–77.86) | 70.08 (44.71–95.44) | 62.97 |
| Small | | | | | | | | | |
| Moulding | 2 | 0.07 (0.02–0.11) | 4.35 (0.13–8.57) | 4.42 (0.24–8.60) | 98.42 | 10.36 (5.31–15.40) | 4.81 (0.54–9.08) | 15.16 (14.39–15.94) | 31.73 |
| Pouring | 2 | 0.08 (0.05–0.12) | 17.74 (14.21–21.27) | 17.82 (14.26–21.39) | 99.55 | 2.70 (2.60–2.81) | 18.39 (14.74–22.05) | 21.09 (17.33–24.85) | 87.20 |
| B | | | | | | | | | |
| Big | | | | | | | | | |
| Moulding | 4 | 0.06 (0.04–0.08) | 3.94 (1.68–5.88) | 4.00 (1.72–5.94) | 98.50 | 1.14 (0.78–1.70) | 7.13 (2.51–11.73) | 8.28 (3.29–12.95) | 86.11 |
| Pouring | 5 | 0.47 (0.17–0.98) | 10.53 (6.93–14.03) | 11.00 (7.44–15.01) | 95.73 | 13.48 (1.25–44.71) | 16.74 (11.90–23.16) | 30.22 (18.48–56.61) | 55.39 |

*Note*: Big indicates the big mould and small indicates the small mould; minimum–maximum are shown inside parenthesis.

total PAH levels. Although the total BaPeq levels of particulate phase and gaseous phase were almost equal between the two industries, the five- and six-ring PAHs contributed the most toxicity to BaPeq levels in Foundry A than those of Foundry B, including BaP, IND, DBA, and Bghip.

Foundry A produces big and small moulds, while only big moulds are produced in Foundry B. The differences in air PAH levels in moulding and pouring areas were therefore further evaluated between the two foundries in Table 3. In Foundry A, a new environmental control system was installed in the manufacturing areas over a year ago. The air sampling showed that in Foundry B, even though there were only big moulding processes were performed, which use more chemical binders-furan resin, the higher PAH levels were found in Foundry A than in Foundry B (7.36 $\mu g/m^3$ and 4.00 $\mu g/m^3$ in the moulding areas, and 36.56 $\mu g/m^3$ and 11.0 $\mu g/m^3$ in the pouring areas, respectively). When comparing the PAH emission between the big moulds and small moulds in Foundry A, a higher level was found in the big mould production process than the small mould. Furthermore, a high variation of the BaPeq level in the two foundries was also found between big moulds and small moulds, as well as those in different foundry industries.

### 3.2. PAH emission in different working departments

The 16 PAH levels in different working departments are shown in Table 4. The higher concentrations of 16 PAH were found in the painting area (95.51 $\mu g/m^3$), pouring area (18.42 $\mu g/m^3$), and inside office (16.48 $\mu g/m^3$); the lower levels were found in the grinding area (2.90 $\mu g/m^3$) and outdoors (2.78 $\mu g/m^3$). Meanwhile, of the 16 PAHs measured in the foundry plants, over 90% were in the gaseous phase in inside and outside offices. Table 5 presents the BaPeq levels of the 16 PAHs in different manufacturing areas of the two foundries. The higher levels of BaPeq were found in the painting area (152.3 $ng/m^3$), the furnace for melting iron (96.9 $ng/m^3$), and the pouring area (37.05 $ng/m^3$); the lower levels were found outdoors (5.74 $ng/m^3$) and in the grinding area (7.91 $ng/m^3$). The gaseous/particulate ratio varied more for BaPeq levels than for 16 PAH levels.

### 3.3. Health risk assessment of PAHs in foundry workers

The cancer risk calculations based on time-weighted average exposure levels of BaPeq of foundries' workers are presented in Table 6. The unit risk of BaPeq was adopted from Nisbet and LaGoy [19], and Lin et al. [23]. The cancer risks of PAH exposure in Foundries A and B were $9.06 \times 10^{-4}$ and $1.09 \times 10^{-3}$, respectively. The risk of gaseous phase and particulate phase PAHs were almost equal in both foundries.

## 4. Discussion

### 4.1. PAH levels in the foundry industries

A previous study that focused on evaluating sources of PAHs in urban soil suggested that foundries were potentially important sources of PAH in the vicinity of urban soil and sediment [21].

When comparing environmental samplings, the air PAHs ranged from 0.022 $\mu g/m^3$ to 156.7 $\mu g/m^3$ in this occupational study, which was obviously higher than those ranged from 44.3 $ng/m^3$ to 129.2 $ng/m^3$ in an urban region of Greece [15], as well as those also higher than PAH levels in the gaseous phase ranged between 6.89 and 124 $ng/m^3$, while in the particulate phase between 0.44 and 13.2 $ng/m^3$ in suburban area of Athens greater area [22].

When comparing the occupational groups, the higher levels were found in the painting department (95.41 $\mu g/m^3$) and the pouring department (18.48 $\mu g/m^3$), and which were also higher

**Table 4**
Average concentrations (μg/m³) of 16 gaseous and particulate PAHs by the working process.

| Department | Moulding | Furnace | Pouring | Shakeout | Grinding | Painting | Resin storage | Office-i | Office-o | Outdoor |
|---|---|---|---|---|---|---|---|---|---|---|
| *N*= | 9 | 7 | 9 | 2 | 5 | 2 | 3 | 2 | 2 | 2 |
| Nap | 3.93 | 9.53 | 16.05 | 5.00 | 2.52 | 89.61 | 6.15 | 15.87 | 7.18 | 2.50 |
| AcPy | 0.44 | 0.45 | 0.70 | 0.06 | 0.06 | 0.73 | 0.41 | 0.18 | 0.14 | 0.05 |
| Acp | 0.02 | 0.11 | 0.10 | 0.04 | 0.07 | 0.09 | 0.05 | 0.07 | 0.06 | 0.02 |
| Flu | 0.21 | 0.20 | 0.44 | 0.03 | 0.02 | 0.49 | 0.23 | 0.08 | 0.12 | 0.03 |
| PA | 0.31 | 0.66 | 0.59 | 0.12 | 0.09 | 3.66 | 0.27 | 0.17 | 0.25 | 0.09 |
| Ant | 0.04 | 0.12 | 0.25 | 0.04 | 0.05 | 0.08 | 0.04 | 0.07 | 0.08 | 0.01 |
| FL | 0.15 | 0.15 | 0.11 | 0.04 | 0.03 | 0.74 | 0.26 | 0.01 | 0.06 | 0.04 |
| Pyr | 0.03 | 0.08 | 0.08 | 0.02 | 0.01 | N.D. | 0.02 | 0.01 | 0.03 | 0.01 |
| BaA | N.D. | 0.04 | 0.02 | N.D. | 0.01 | 0.04 | N.D. | N.D. | 0.01 | 0.01 |
| CHR | 0.01 | 0.02 | 0.01 | N.D. | N.D. | N.D. | 0.01 | N.D. | N.D. | N.D. |
| BbF | 0.02 | 0.02 | N.D. | N.D. | N.D. | N.D. | 0.01 | 0.01 | 0.01 | N.D. |
| BkF | N.D. | 0.01 | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. |
| BaP | N.D. | 0.05 | 0.01 | N.D. | N.D. | 0.05 | N.D. | N.D. | N.D. | N.D. |
| IND | 0.01 | 0.04 | 0.01 | 0.03 | 0.03 | 0.01 | N.D. | 0.01 | 0.01 | 0.02 |
| DBA | N.D. | 0.02 | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. |
| Bghip | 0.03 | 0.02 | 0.01 | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. | N.D. |
| Particulate PAHs | 0.10 (0.06) | 0.42 (0.51) | 0.43 (0.40) | 0.30 (0.32) | 0.30 (0.54) | 0.08 (0.08) | 0.14 (0.08) | 0.11 (0.01) | 0.41 (0.43) | 0.04 (0.03) |
| Gas-PAHs | 5.11 (3.65) | 11.11 (10.81) | 17.99 (17.96) | 5.10 (5.27) | 2.59 (1.98) | 95.43 (86.62) | 7.32 (8.70) | 16.37 (20.70) | 7.55 (2.18) | 2.74 (2.12) |
| Total PAHs | 5.21 (3.66) | 11.53 (10.79) | 18.42 (18.22) | 5.40 (5.59) | 2.90 (1.90) | 95.51 (86.54) | 7.45 (8.74) | 16.48 (20.68) | 7.96 (1.75) | 2.78 (2.14) |
| Gas% | 98.12 | 96.36 | 97.67 | 94.49 | 89.47 | 99.92 | 98.17 | 99.32 | 94.85 | 98.69 |

*Note*: Office-i means inside the office and Office-o means outside the office; N.D.: non-detected; the standard deviation is shown inside parenthesis.

**Table 5**
Mean BaPeq levels (ng/m³) of 16 gaseous and particulate PAHs by the working process.

| Department | Moulding | Furnace | Pouring | Shakeout | Grinding | Painting | Resin storage | Office-i | Office-o | Outdoor |
|---|---|---|---|---|---|---|---|---|---|---|
| *N*= | 9 | 7 | 9 | 2 | 5 | 2 | 3 | 2 | 2 | 2 |
| Nap | 3.93 | 9.53 | 16.05 | 5.00 | 2.52 | 89.61 | 6.15 | 15.87 | 7.18 | 2.50 |
| AcPy | 0.44 | 0.45 | 0.70 | 0.06 | 0.06 | 0.73 | 0.41 | 0.18 | 0.14 | 0.05 |
| Acp | 0.02 | 0.11 | 0.10 | 0.04 | 0.07 | 0.09 | 0.05 | 0.07 | 0.06 | 0.02 |
| Flu | 0.21 | 0.20 | 0.44 | 0.03 | 0.02 | 0.49 | 0.23 | 0.08 | 0.12 | 0.03 |
| PA | 0.31 | 0.66 | 0.59 | 0.12 | 0.09 | 3.66 | 0.27 | 0.17 | 0.25 | 0.09 |
| Ant | 0.37 | 1.25 | 2.47 | 0.43 | 0.54 | 0.75 | 0.39 | 0.72 | 0.80 | 0.15 |
| FL | 0.15 | 0.15 | 0.11 | 0.04 | 0.03 | 0.74 | 0.26 | 0.01 | 0.06 | 0.04 |
| Pyr | 0.03 | 0.08 | 0.08 | 0.02 | 0.01 | N.D. | 0.02 | 0.01 | 0.03 | 0.01 |
| BaA | 0.38 | 3.73 | 2.15 | 0.26 | 0.59 | 3.54 | 0.21 | 0.23 | 0.89 | 0.69 |
| CHR | 0.07 | 0.17 | 0.13 | 0.01 | 0.01 | 0.03 | 0.05 | N.D. | 0.04 | N.D. |
| BbF | 1.52 | 1.82 | 0.48 | 0.20 | 0.19 | 0.28 | 0.89 | 0.82 | 0.69 | 0.03 |
| BkF | 0.38 | 1.29 | 0.36 | 0.09 | 0.06 | 0.04 | 0.37 | 0.01 | 0.01 | 0.04 |
| BaP | 3.54 | 51.24 | 6.96 | 0.95 | 0.83 | 50.09 | 0.34 | 0.04 | 0.04 | 0.05 |
| IND | 1.45 | 4.41 | 1.45 | 2.51 | 2.55 | 0.98 | 0.39 | 1.31 | 1.20 | 1.67 |
| DBA | 3.38 | 21.60 | 4.82 | 0.96 | 0.30 | 1.24 | 3.86 | 0.21 | 0.30 | 0.35 |
| Bghip | 0.26 | 0.20 | 0.14 | 0.02 | 0.03 | 0.03 | 0.03 | 0.01 | 0.01 | 0.02 |
| Particulate PAHs | 9.62 (9.75) | 65.57 (78.66) | 13.85 (15.71) | 3.52 (3.24) | 3.33 (2.61) | 2.03 (0.14) | 5.84 (5.91) | 2.54 (0.81) | 2.89 (1.74) | 0.94 (0.59) |
| Gas-PAHs | 6.82 (4.21) | 31.33 (44.22) | 23.19 (20.92) | 7.23 (3.05) | 4.58 (3.59) | 150.27 (10.60) | 8.09 (8.88) | 17.21 (20.33) | 8.93 (1.50) | 4.80 (0.68) |
| Total PAHs | 16.44 (10.04) | 96.90 (83.78) | 37.05 (25.43) | 10.75 (6.29) | 7.91 (1.74) | 152.30 (10.47) | 13.93 (7.09) | 19.75 (19.52) | 11.83 (0.24) | 5.74 (0.09) |
| Gas% | 41.46 | 32.33 | 62.61 | 67.26 | 57.91 | 98.67 | 58.06 | 87.15 | 75.54 | 83.63 |

*Note*: Office-i means inside the office and Office-o means outside the office; N.D.: non-detected; the standard deviation is shown inside parenthesis.

**Table 6**
Time-weighted average exposure levels of total BaPeq and the cancer risk of workers exposed to gaseous/particle phase PAHs between Foundries A and B.

| | Foundry A | Foundry B |
|---|---|---|
| Unit risk $(ng/m^3)^{-1}$ [a] | $7.00 \times 10^{-5}$ | $7.00 \times 10^{-5}$ |
| BaPeq ($ng/m^3$) | | |
| Gas phase | 7.02 | 8.44 |
| Particle phase | 5.91 | 7.07 |
| Cancer risk[b] | | |
| Gas phase | $4.92 \times 10^{-4}$ | $5.91 \times 10^{-4}$ |
| Particle phase | $4.14 \times 10^{-4}$ | $4.95 \times 10^{-4}$ |
| Total cancer | $9.06 \times 10^{-4}$ | $1.09 \times 10^{-3}$ |

[a] The unit risk was adopted from Lin et al. [23].
[b] Risk of cancer= air levels ($\mu g/m^3$) × unit risk $(\mu g/m^3)^{-1}$.

than the PAH concentration (461.8–935.6 $ng/m^3$) near the continuous casting area of an electric steel foundry [1]. Additionally, these levels were higher than the airborne PAH concentrations (sum of 15 selected PAH compounds: 9.6–11.2 $\mu g/m^3$) in the casting, machine moulding, and shakeout departments [2]. As compared to the samplings in the sinter plant, the concentrations in these working zones were obviously higher than the concentrations in the raw material inlet, sintering grate, rough roll shredder and control room (8.37–30.4 $\mu g/m^3$) [23].

Meanwhile, a previous study conducted in iron foundries found that workers engaged in different stages of the production of iron casts were exposed to carcinogenic PAHs, especially in casting of moulds [24]. The BaPeq levels were high in resin storage and moulding areas in the current study, which was not totally consistent with other studies [2,24]. The reasons for the difference may be interpreted as follows: (1) many chemicals, such as chemical binding-furan resin, present in the resin storage areas. (2) The melting and pouring processes may be the major sources of PAHs due to the high temperature used during these processes. However, the cover on top of the furnace is usually closed and is only opened when the melting process is completed. (3) The pouring process is a short-term process, and the moulding areas are where the moulds cool down after the pouring is completed. Therefore, the pouring and moulding processes cannot be separated completely. The occupational hazards of PAHs cannot be neglected if the worker's job integrates the moulding, pouring, and melting processes.

### 4.2. The PAH levels in the two foundries

This study was conducted in two typical foundry plants in central Taiwan. Foundry A typically uses an induction furnace for melting metal, and Foundry B uses a cupola for melting metal. The production of Foundry A includes big and small moulds, but only big moulds are produced in Foundry B. Another difference between the two foundries is that furan resin and silicate sands are used in Foundry A, and only furan resin is used in Foundry B. No significant difference in particle concentration was found between the two foundries, whereas a difference was found for the total levels of 16 PAHs. When expressed in BaPeq, the gaseous/particulate phases were almost equal in BaPeq levels. Therefore, these data suggest that the gaseous phase may have a major effect on the distribution of BaPeq in foundries. Meanwhile, a previous study indicated that variations of PAH levels can be attributed to chemical binders of iron casting moulds [25], and a leaching study also indicated that PAH concentrations varied between green sand and chemical binder spent sands in addition to the variation according to whether the bindings were made of phenolic/ester or furan/acid [16]. From Table 3, we can see that the operating process and products may influence the use of foundry sand and binding chemicals, which are important factors to affect the PAH components in foundries.

### 4.3. Gas/particle phase of PAHs in foundries

The gaseous phase contributed 98.67% and 96.38% of the total 16 PAH levels in Foundries A and B, respectively. These values were equal to 98.4% and 98.8% contributions that were found in the workplace atmospheres of iron foundries and sinter plants, respectively [13,23]. When comparing the gas proportion indoors and outdoors, 98.65% of PAHs were found in the gaseous phase in outdoor samples, which was comparable to data that suggested that gas phase contributed to almost 90% of PAHs in suburban areas [22], but was higher than the gaseous phase contributions in an urban atmosphere [15]. Over 90% of 16 PAHs in some working areas was gaseous phase, including those in manufacturing areas and inside and outside offices. The amount of PAHs in the gaseous phase in the present study was higher than the levels inside an iron foundry (77%) [12]. Meanwhile, Knecht et al. found that the gaseous phase contained on average threefold more carcinogenic four- and five-ring PAHs than the particle phase. However, this distribution was only found in some workplaces, such as the shakeout, grinding, painting, resin storage and outdoor areas in this study. In addition, Shimmo et al. indicated that the proportion of the gaseous concentration of each PAH varied. For example, 100% of Ay was found in the gaseous phase, and 100% of DBA was found in the particulate phase [14]. Shimmo et al. also indicated that total particulate PAH concentrations were higher in particles smaller than 440 nm and 2.5 μm. Meanwhile, it has been suggested that shifts in gaseous/particulate distribution are due to differences in ambient temperature, which accounts for the seasonal variation of the concentration of PAHs in particles. Because high temperatures are used in foundry plants, possible influencing factors may include particle size and high temperatures in working areas, such as those happened in the moulding, melting, and pouring areas.

### 4.4. Risk assessment of PAHs

Although the average total BaPeq exposure levels were lower than the permissible exposure limit set by the Occupational Safety and Health Administration (OSHA, 8-h time-weighted average: 0.2 $mg/m^3$), the lung cancer risks associated with the above PAH exposures ranged from $9.06 \times 10^{-4}$ to $1.09 \times 10^{-3}$, which were higher than those in sinter plant workers ($3.18 \times 10^{-5}$ to $4.98 \times 10^{-5}$) and temple workers ($10^{-6}$ to $10^{-4}$) who had occupational PAH exposure [23,26]. The lung cancer risk due to gaseous phase PAH exposure was much higher than that of particulate phase PAH exposure in the workers of oil mists in a fastener manufacturing industry, which showed an almost equal contribution of risk for exposure to the gaseous phase or particulate phase PAHs [27]. Meanwhile, the lung cancer risk does reflect a previous study that reported relative risk of lung and respiratory cancer in the workers with PAH exposure in iron and steel foundries (1.40, 95% CI 1.31–1.49) [8]. Additionally, this correlates with our previous study that demonstrated high oxidative damage in foundry workers [28,29].

Therefore, future studies should follow up to efficiently develop biological markers to show the effect of PAHs on the lung and respiratory tract [8], including bronchus and lung impairment in foundry workers.

## 5. Conclusion

The present study shows that total PAH levels in the selected areas of the manufacturing process are higher than outside the foundry industry. The higher PAH levels are also found inside

offices, which indicate that large quantities of PAHs are leached from the manufacturing areas to administrative areas. This can be explained by the incorrect layout of exhaust equipment in the manufacturing areas because the exhaust outlet is near the upper the office. Therefore, it cannot be overlooked that administrative workers in foundries are also exposed to PAHs emitted from the foundry operating processes. Gaseous phase PAHs comprise the majority of total PAHs, and the cotton masks that the workers use cannot effectively prevent gaseous PAHs exposure of the workers in the painting, melting, and pouring districts. Moreover, the workers at foundry plants have a significantly higher cancer risk based on the ambient BaPeq levels. Together with our previous report, these data indicate that elevated oxidative damages are found in foundry workers. How to utilize biological effect markers to detect the precursor of lung cancer will be important in further studies.

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