

出國報告（出國類別：其他）

## 出席上海第四屆生物醫學工程與生物 技術國際學術會議出國報告

服務機關：核能研究所

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出國期間：104年8月17日~104年8月21日

報告日期：104年9月21日



## 摘 要

本次公差主要目的是赴大陸上海市參加「第四屆生物醫學工程與生物技術國際學術會議，The 4th International Conference on Biomedical Engineering and Biotechnology (簡稱 ICBE2015)」。

聆聽及學習大會邀請五位傑出學者專題演講、分組口頭報告論文發表及參觀與討論海報論文發表。而筆者亦提出一篇壁報論文和與會者討論、說明應用層析質譜分析藥物相關衍生物並探求原因之論文研究心得。並介紹本所核醫藥物研究活動及成果。ICBE2015 於 8 月 18 至 21 日舉行，參與人員國籍以大陸最多，其它來自日、韓、新加坡、馬來西亞、土耳其及歐洲等國家，台灣約有 10 位左右與會，共約有 250~300 人參加。大會主題包含: I. 生物醫學工程、超音波與生物醫學信號處理、II. 健康系統、生物資訊學與計算生物學、III. 生物力學與生物機械工程學、IV. 生物材料、V. 其他。題目包括生物醫學相關材料及藥物、影像獲得與處理、生物資訊與計算機應用等。由會議獲得訊息對於本所未來新研究方向之規劃啟發更多可能性。

# 目 次

## 摘 要

(頁碼)

一、目 的 . . . . .	1
二、過 程 . . . . .	2
三、心 得 . . . . .	15
四、建 議 事 項 . . . . .	17
五、附 件 . . . . .	18

# 一、目的

「生物醫學工程與生物技術國際學術會議」(International Conference on Biomedical Engineering and Biotechnology, ICBE) 每年舉辦一屆。2015 年為第四屆，訂於 8 月 18 日至 21 日在上海召開。前三屆依次分別在澳門、武漢、北京舉行。參加人數自首屆的 200 餘人逐年增加，今年約 250-300 人與會。大會主旨在生物醫學工程、生物醫學材料、生物醫學影像與信號處理、生物力學工程等多個學科領域的學者、研究人員，提供前瞻性研究交流、討論的國際平台，以達到學術成果共用，成果應用的目的。

核能研究所長期積極推動同位素的生物醫學應用，包括放射同位素用於疾病診斷、放射治療等。疾病診斷方面，又可分為利用伽瑪射線的單光子放射斷層掃描 (Single Photon Emission Computed Tomography, SPECT) 及正子放射斷層掃描 (Positron Emission Tomography, PET)、磁共振造影 (magnetic resonance imaging, MRI) 等儀器之造影劑，用於中樞神經病變診斷、肝功能評估等。放射治療方面則研發結合栓塞及放射效應治療肝癌等藥物。分別針對螯合配位子的開發設計與合成製備、同位素核種的生產製備、造影劑動物實驗、核醫藥物生產、輻射偵測軟硬體精進等技術層面分頭研究發展，期能開發低劑量、高靈敏度與專一性的核醫藥物、偵檢儀器，以早期診斷、發現病灶、給予有效治療，為國人健康貢獻心力。這些研究屬於生物醫學材料工程相關領域。化學組藥物合成實驗室及藥物鑑定分析實驗室在本研討會發表 2 篇研究成果壁報論文，題目分別為「The synthesis of MN-16ET, DODA, DOTA, and NOTA derivatives as the therapeutic labeling ligand of liver cancer」、「Forced degradation characterization of H<sub>3</sub>MN-16ET using liquid chromatography-tandem mass spectrometry」，本大會歸類於生醫材料部分。由陳威希代表參加研討會說明論文內容，介紹本所研究放射治療及分子影像藥物之研發能力。此外，聆聽學術演講、口頭論文發表、參觀壁報發表。由本會議獲得最新市場資訊及未來發展趨勢，並學習生醫工程相關知識，對本所未來研究發展具啟發及借鏡之意義。

## 二、過 程

### (一) 行程說明

公差行程摘要：

日 期	出發	抵達	停留/工作地點與工作內容
8 月 17 日 星期一	桃園國 際機場	上海浦 東機場	行程：由台北市出發抵達上海市
8 月 18 日~20 日 星期二~四	上海住 宿旅館	上海研 討會場	參加 ICBEB 研討會
8 月 21 日 星期五	上海虹 橋機場	台北松 山機場	行程:由上海市返抵台北

2015 年第四屆「生物醫學工程與生物技術國際學術會議」(International Conference on Biomedical Engineering and Biotechnology, ICBEB2015)在上海市長寧區的美崙飯店(Royalton Hotel)於 8 月 18 日~20 日舉辦，議程如附件一所示。筆者出席本次研討會，代表本所發表成果海報 2 篇(分別由藥物鑑定分析實驗室、藥物合成實驗室完成 1 篇)。



圖 1. 第四屆「生物醫學工程與生物技術國際學術會議」會場

## (二) ICBEB-2015 會議

會議主題包含生物醫學工程、生物醫學材料、超音波與生物醫學信號處理、生物醫學影像、生物力學與生物機械工程、健康系統、生物資訊學與計算生物學等生醫科技領域提供技術交流與應用之平台。以建構改善人類健康、疾病診斷與治療、復健等之科技發展。邀請 5 位分別來自美國(2 位)、新加坡、英國、巴西學者專題演講各 45 分鐘，隨後進行 2 梯次共約 150 篇以上壁報論文發表、說明與討論壁報內容。第二天口頭簡報論文發表有 57 位，分為 3 個主題會場(生醫工程、生醫影像信號處理、生醫材料)同時進行。每個題目以 10 分鐘英文簡報及 3-5 分鐘問題討論為限。來自中國(主要與會者國籍)，俄羅斯，韓國，馬來西亞，日本，土耳其等各國的醫院工作者、大學研究人員、產業界等約有 250 位以上人員參加，台灣約有 10 位與會。論文主題有電腦運算於生醫影像應用，超音波影像應用、SPECT 及 MRI 影像改善，造影劑研發，骨髓幹細胞、藥物輸送奈米微胞等。化學組藥物鑑定分析實驗室的成果發表壁報論文一篇「Forced degradation characterization of H<sub>3</sub>MN-16ET using liquid chromatography-tandem mass spectrometry」，為本所研發 Re-188-MN16ET 肝癌治療藥物之主成分前驅物：保護基-H<sub>3</sub>MN-16ET 之強迫降解與產物研究，以評估前驅物安定性、降解變質原因與降解物身分，藉以擬定有效期、保存條件、與可能的降解物對藥物使用上之影響。此研究成果並已彙整撰寫論文，將投稿 SCI 期刊。這項研究也是 Re-188-MN16ET 肝癌治療藥物申請臨床試驗所需之文件，具有重要意義。論文摘要如附件二，壁報如附件三。此外，並代表本組藥物合成實驗室 張瑜 博士所提壁報論文「The synthesis of MN-16ET, DODA, DOTA, and NOTA derivatives as the therapeutic labeling ligand of liver cancer」的說明。並向與會者簡介本所在同位素生醫藥物應用研究現況。圖 2 為陳威希與本組所發表壁報 2 篇。

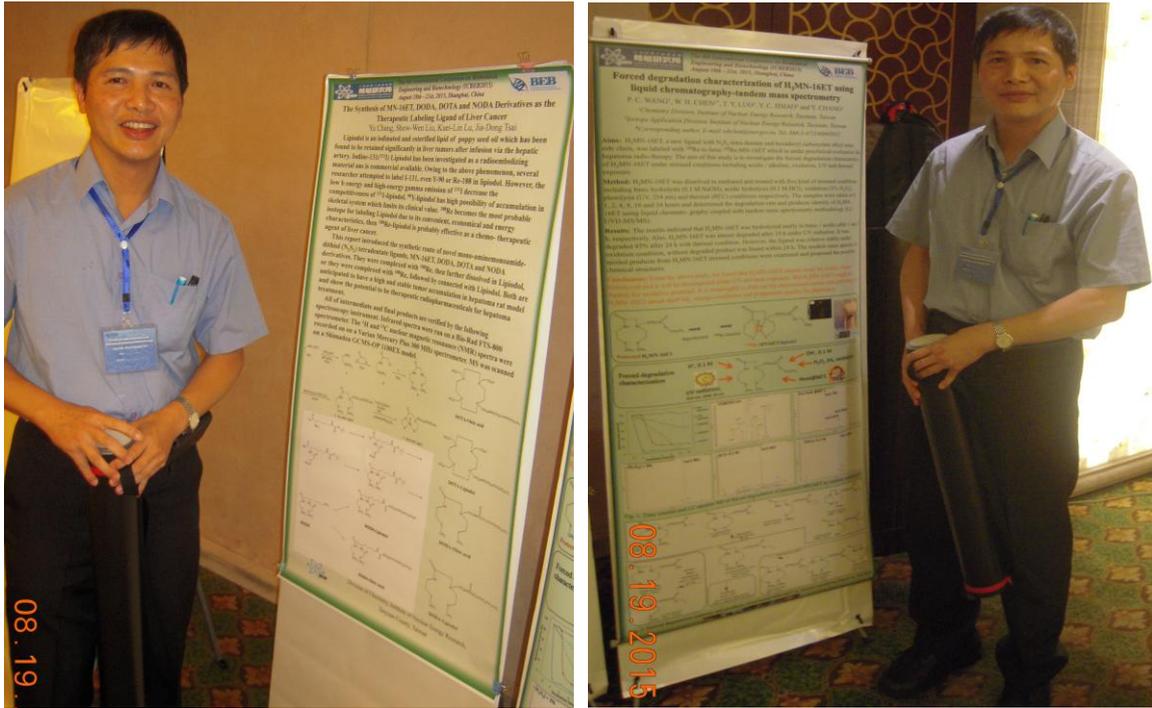


圖 2. 發表壁報現場

### 會議摘要

#### 1. 五位邀請專題報告講員及內容摘要:

(1)Dr. Edward J. Ciaccio, Columbia University, USA。專長為應用電腦運算研究生醫工程與資訊。研究焦點是心臟電生理信號分析。報告題目「An LMS Algorithm for Characterization of BioSignal Shape」



說明生醫影像信號處理藉 Least mean squares (LSM, 最小均方根)特徵運算法可改善影像品質。

(2)Dr. Ng Yin Kwee, Nanyang Technological University, Singapore。專長為熱影像、生醫工程、乳癌偵測、計算流體力學。報告題目「Computer-Aided Diagnosis of Myocardial Infarction Using



Ultrasound Images with Second-Order Statistics, DWT and HOS Methods: A Comparative Study」說明利用超音波影像及二階統計、離散小波變換 (Discrete Wavelet Transform, DWT)、高階光譜 (Higher Order Spectra, HOS)等運算方法於電腦輔助診斷心肌梗塞的研究成果。超音波影像及電腦輔助診斷心肌

梗塞程度，藉人工智慧技術，幫助臨床醫師及時採取正確治療對策，改善傳統使用二維心電圖，因醫師經驗解讀差異之缺點。研究中比較 80 位心肌梗塞病患及 80 位正常人分別各獲取 1600 張超音波影像，利用上述電腦影像運算比對方法，歸納分析特徵，用於心肌梗塞病患診斷，準確率達 98.8%，專一性 99%，靈敏度 98.5%。顯示對心臟科醫師正確診斷心肌梗塞確有助益。

(3)Dr. Daniel Elson, Imperial College, London, UK. 研究方向為內視鏡光學技術的研發應用於外科影像，光學技術包括偏極光解析影像、螢光、雷射散佈點對比影像。報告題目「Surgical Imaging, Biophotonics and Endoscopy」。說明應用影像與光學技術整合於內視鏡以輔助手術決策。



(4)Prof. Zheng-Rong Lu, 呂政榮(E-mail: zxl125@case.edu)。Department of Biomedical Engineering, Case Western Reserve University, USA. 畢業於中國蘭州大學化學系，研究領域為新分子影像技術及藥物傳送



系統的設計與應用於診斷與治療疾病：1. Biodegradable macromolecular MRI contrast agents 2. Targeted MRI contrast agents for specific cancer imaging 3. Image-guided minimally invasive cancer treatment 4. Design and development of effective drug delivery systems。報告題目「Early Detection and Treatment of Metastatic Breast Cancer」。設計研發  $Gd^{3+}$  的 MRI 顯影劑以偵測轉移癌生物標記。此顯影劑（包括  $Gd(DTPA)^{2-}$ ,  $Gd(DTPA-BMA)$ ,  $Gd(DOTA)^-$ ,  $Gd(HP-DO3A)$  等）、超順磁鐵氧化物奈米粒子(SPIO)。這些順磁化合物與標的單株抗體、醣類分子專一的與生物標記結合，如圖 3。腫瘤小至 0.5 mm 都可高對比顯影，靈敏的診斷微轉移癌細胞。此外也研發多功能藥物輸送系統以傳送治療的 siRNA (Small interfering RNA, 是長度 20 到 25 個核苷酸的雙股 RNA，參與 RNA 干擾現象，



以專一性的方式調節疾病相關基因的表達、使有效治療疾病)，由動物實驗知對轉移性乳癌具有療效。筆者由呂教授簡報及研究內容，認為與本所研發方向具有相關，特向呂教授致意、簡介本所核醫藥物研發方向、邀請有機會訪問台灣時蒞所演講指導，獲正面回應。

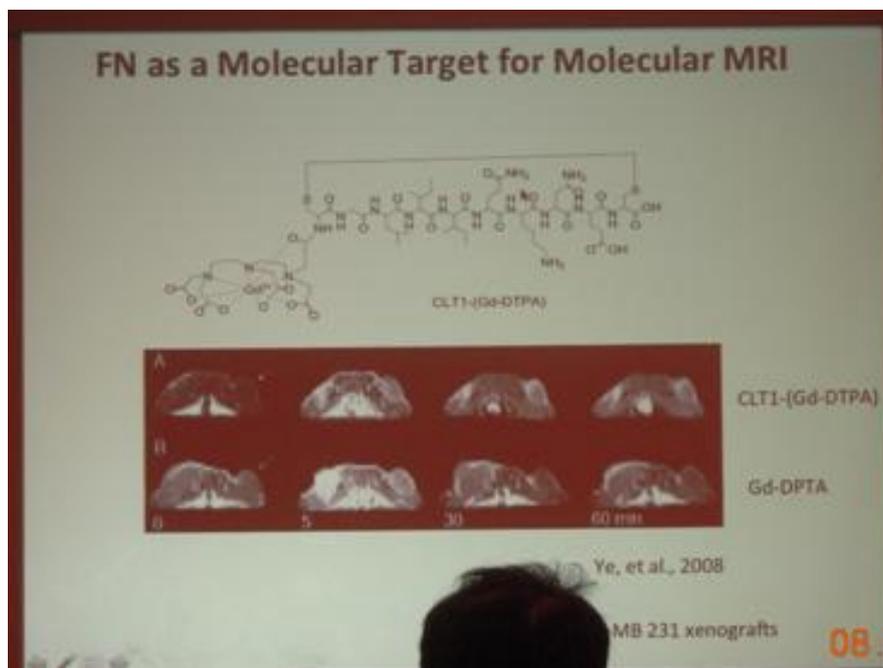


圖 3. 順磁化合物與標的單株抗體、醣類分子專一的與生物標記結合

(5) Prof. David De Jong, Genetics Department, Ribeirao Preto Medical School, University of São Paulo, Brazil. 研究方向為遺傳學及昆蟲學者。報告題目「The Importance of Scientific Journals for



Advancement in Biomedicine」。說明現今的科研進展及知識傳遞、應用都有賴於科研期刊的出版。故研究人員的工作成果若希望發揮影響力，撰寫論文投稿期刊是必要的。期刊編輯群收到投稿後先評估文稿適合發表的可能性，轉予文稿審查人(peer reviewer)，評估研究執行妥善、適宜雜誌刊登、指正誤謬等。演講內容介紹投稿期刊作者應注意事項及論文撰寫要點，對年輕科研人員整理論文甚有助益。

## 2. 大會壁報論文發表

本研討會由國際期刊出版社 IOS Press 贊助，接受發表的論文全文或摘要會後依論文屬性分類刊登於出版社旗下期刊: Bio-medical Materials and Engineering (BMME, Impact factor: 1.09)、Human Vaccines & Immunotherapeutics (IF: 2.37)、Basic & Clinical Pharmacology & Toxicology (BCPT, IF: 2.34)、Biomedical Signal Processing and Control (IF: 1.42)。筆者投稿壁報論文摘要為核醫藥物原料之安定性與強迫降解性質研究，將刊登於 BCPT。文章並可由網路檢索取得。可增加被國際研究人士搜尋參考的機會。但也因期刊刊登原因，大會資料手冊不提供口頭報告及壁報發表論文摘要等資料，且資料冊目錄所列論文題目並未包含所有發表論文，是令人不滿意的缺點。如圖 4 所示為筆者與大會秘書小姐連繫詢問會議論文集摘要之答覆。因此必須稍後瀏覽上述期刊網頁，查詢出版專刊之發表文章才能獲得發表壁報論文資料。



圖 4. 大會秘書處答覆論文摘要將於期刊出版，不收錄於大會論文集

將部分論文發表資料討論如下。

- (1). Suaiman, Ghazali 等提出題目 [Superparamagnetic calcium ferrite nanoparticles synthesized using a simple Sol-gel method for targeted drug delivery]. (馬來西亞) 全文發表於 Bio-Medical Materials and Engineering 26 (2015) S103–S110。利用

Sol-gel 方法製備具超順磁性的  $\text{CaFe}_2\text{O}_4$  奈米微粒，用於標靶藥物輸送。Sol-gel 方法的成本低，易操作，得到單分散性(monodispersity)，純無定型相(pure amorphous phases)，粒徑一致，因奈米尺寸、超順磁性及生物相容性，適用於以體外磁場引導選擇性精確輸送藥物到達癌細胞起治療作用。藥物負載於磁性奈米微粒注入病患體內，經血管流動及磁場引導到癌細胞。

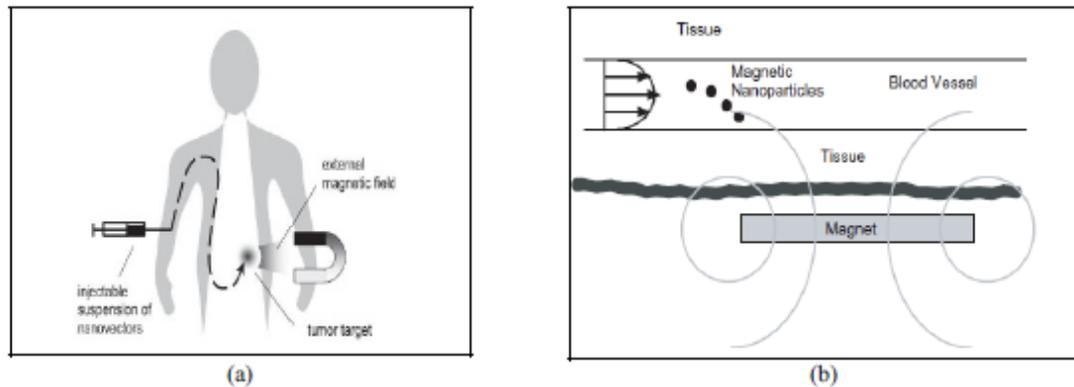
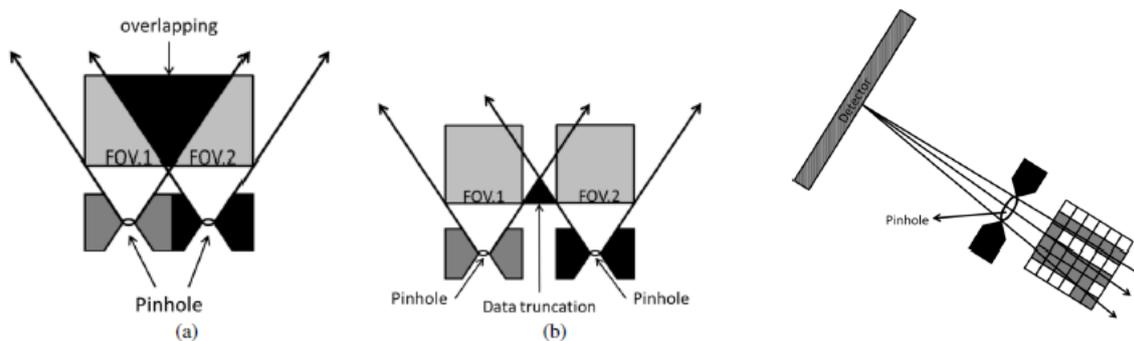


Fig. 1. Drug Delivery system (a) The mechanism of magnetic-field guided drug delivery system, (b) Cross sectional view of the particle trapping mechanism inside the blood vessel

- (2). 台灣清華大學生醫工程與環境科學系博士研究生黃柏嘉提出 [Fast iterative reconstruction for helical pinhole SPECT imaging]。生醫影像處理技術。針孔 SPECT 影像對小動物體內病變觀察是常用的工具。而這僅能掃描近似立方體且視野極有限。本研究設計裝置改善影像擷取方式使能處理較大物體獲較佳影像品質。文章已發表於 Bio-medical Materials and Engineering 26 (2015) S1371。



- (3). 台灣國家衛生研究院生技與藥物研究所 黃中瑜提出 [Discovery of bone marrow stem cell mobilizers with kidney damage protection activity] 骨髓造血幹細胞負責體內紅血球，血小板，白血球及免疫細胞的製造。骨髓造血幹細胞具

高度分化成為不同功能的細胞與組織。研究發現成熟骨髓細胞能分化成為多種器官細胞，如肝，腎，肺，皮膚及腸胃道等。例如腎臟組織受損後再生可由骨髓幹細胞分化再生而修補。

- (4). 台灣大學張恆華助理教授研究生提出(醫學影像處理) [Automatic brain MR image denoising based on texture feature-based artificial neural networks] 以人工智慧神經網路自動化移除磁振影像雜訊診斷腦部病變之研究。文章已發表於 Bio-medical Materials and Engineering 26 (2015) S1275。

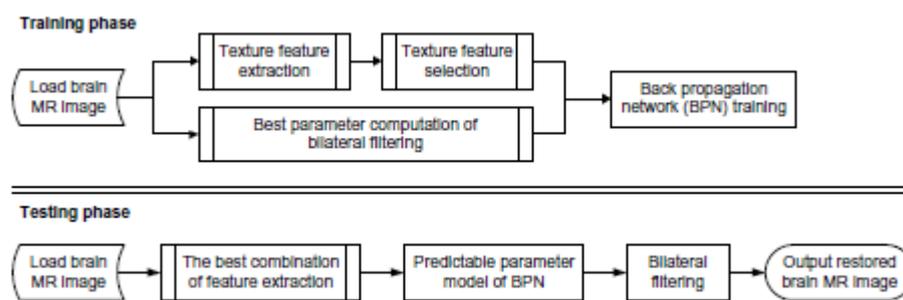
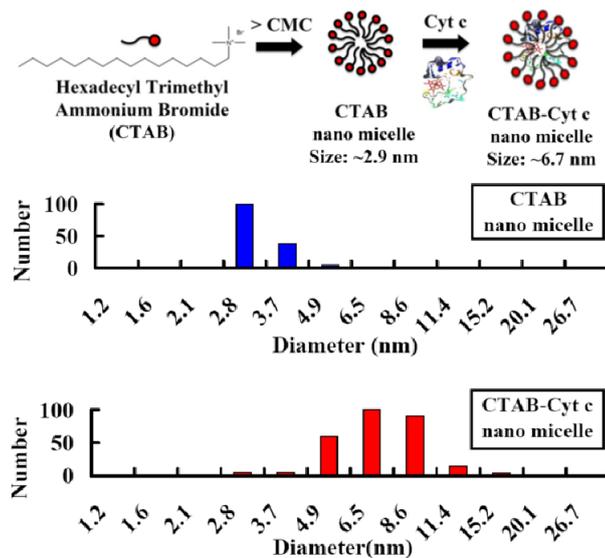


Fig. 1. Flowchart of the proposed automatically denoising scheme.

- (5). 中國河南大學 Tian Yang 提出[A novel self-assembled nano micelle as a highly efficient artificial peroxidase based on hexadecyl trimethyl ammonium bromide and cytochrome c] 文章已發表於 Bio-medical Materials and Engineering 26 (2015) S73。利用界面活性劑 hexadecyl trimethyl ammonium bromide (CTAB) 生成的奈米微胞及取自牛心臟 cytochrome c 製成的高催化效率過氧化酶，以 UV 光譜儀及 Circular Dichroism (CD) 圓二色性光譜儀研究奈米微胞-Cyt c 過氧化酶性質，結果顯示 Cyt c 酶被 CTAB 自組合奈米微胞包覆後，Cyt c 酶的疏水性 heme group 部分更為外露使其氧化沒效率提高，這可取代常用的 horseradish peroxidase (辣根過氧化酶，在生化領域有廣泛地應用，因為它具有將微弱信號放大及增強靶標分子可檢測度的能力)。



Scheme. 1. Preparation process of CTAB-Cyt *c* nano micelle (AP).

### 3. 部分大會口頭論文發表摘要討論如下

#### (1). Dr Biqiong Chen [Biopolymer graphene nanocomposite microneedles



for transdermal] 陳教授發展生物可分解及相容的石墨烯奈米材

料用於經皮膚吸收之藥物。生物相容及可分解材質有幾丁聚醣(chitosan, 來自甲殼素)。與石墨烯結合後改變幾丁聚醣的性質，使含約 1~2% 石墨烯適合於經皮膚藥物給藥之劑型材料。幾丁聚醣含石墨烯具有導電性，可用於電脈衝穿孔(electroporation)或離子導入法(iontophoresis)以傳遞藥物之應用。石墨烯含量與藥物釋放速率有關。

#### (2). Prof. Ildoo Chung 韓國釜山大學 [Biodegradable nanoporous microspheres for

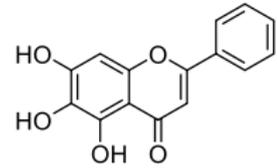
controlled drug delivery system] 控制藥物輸送技術在藥物劑型設計及給藥

過程是重要的一環，結合生物可分解及奈米微孔洞、微粒材料製造特性用於緩釋劑型或給藥途徑應用可增益藥效及擴大用途。生物相容且可分解材料一般為多醣類(例如幾丁聚醣、海藻糖類)，聚酯類(如聚乳酸酯)等，其具有許多活性官能基可修飾改質且可與藥物分子鍵結，緩慢分解釋出，或保護藥物通過胃酸分解等。多醣類奈米微孔洞開放，分子易進出、表面積大，提高藥物生體可用利率及承載藥物容量。

(3). Juan Liu 中國重慶西南大學 [Antibacterial, anti-inflammatory, and antioxidant effects of Yinzhihuang injection] 文章已發表於 Bio-medical Materials and Engineering 26 (2015) S2123。

實驗證明中藥材茵樞黃(注射液：作為退黃降肝酶的治療新生嬰兒黃疸藥物，主要有效成分是

flavonoid baicalein，異黃酮類，結構如圖)，對鴨，小鼠及大鼠實驗對象具有抗發炎，治療微生物感染，抗氧化等效應。



(4). Prof. Kadir Tufan 土耳其 [Analysis of nervous fiber, muscle and blood vessels using their ultraviolet near infrared reflectance characteristics] 文章已發表於

Bio-medical Materials and Engineering 26 (2015) S2179 神經系統受傷後可導致神經組織不可逆的症狀，因為神經細胞再生能力的限制。故研發易於應用的方法以自肌肉與血管之間分離神經纖維是重要問題。本研究目標為開發可靠而容易的測定神經纖維結構差異之方法，作者分析 230 – 1000 nm 波長對肌肉，血管及神經組織的反射光源，發現神經纖維對波長 400 ~600 nm 有較高反射強度，如下圖。研究證明光反射能幫助區分並分離神經組織，具實際應用於手術儀器之可行性。

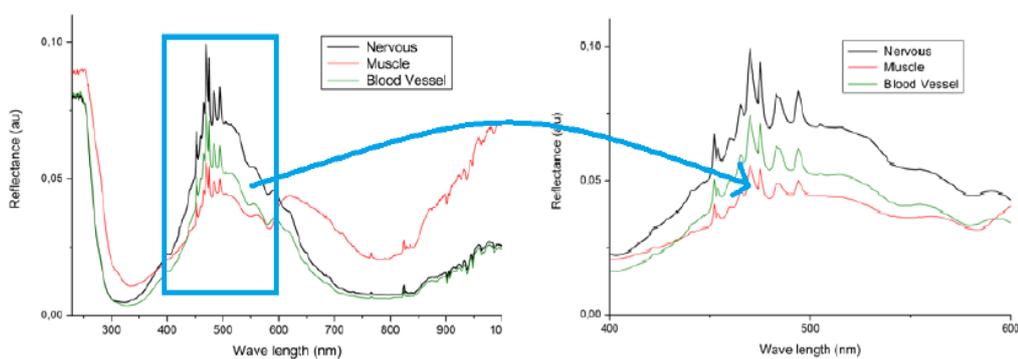


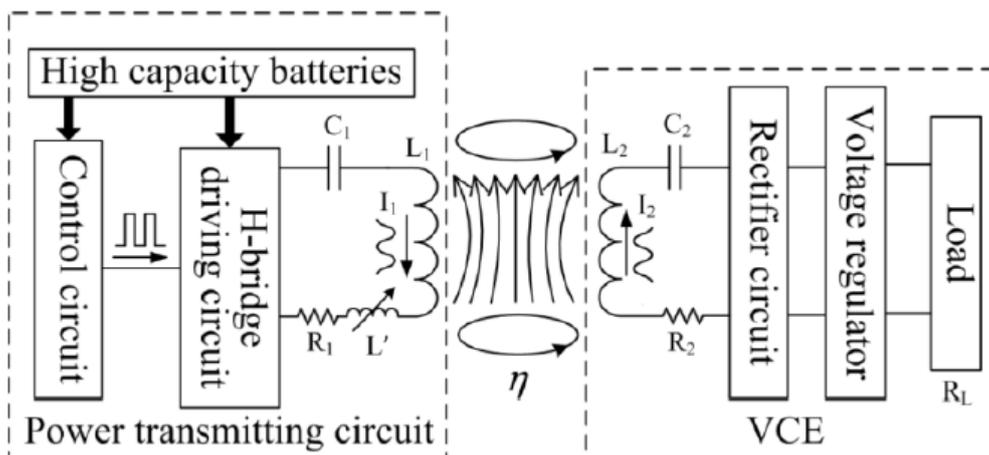
Fig. 2. Average value of tissues for 230 nm – 1000 nm (a) and focus on the vulnerable wavelength range (400 nm – 600 nm) (b).

(5). Prof. Yu Shi, 中國上海交通大學 [A portable wireless power transmission system for video capsule endoscopes] 文章已發表於 Bio-medical Materials and Engineering 26 (2015) S1721 視訊膠囊內視鏡(video capsule endoscopes, VCE) 是將微小攝像鏡頭及無線傳輸信號設備整合以透明材質

包覆成微膠囊形狀，內視鏡檢驗病患經口吞入，經過食道及消化道時攝取影像，以無線通訊將影像訊號傳送顯示螢幕並記錄，藉以觀察消化道病變，並改善傳統消化道內視鏡病患的不適感。已實際應用於醫院診查。膠囊內構造為：光罩，攝影鏡頭，光源，影像晶片，電池，傳輸器，天線，重量約 3-4 g，如圖。  
牟聯·小腸疾病診斷之新紀元--膠囊內視鏡 [www.24drs.com/consumer/event/show/1/images/vod.pps](http://www.24drs.com/consumer/event/show/1/images/vod.pps)



本研究則討論可攜式無線電源傳送(protable wireless power transmission, PWT)技術以解決 VCE 以鈕扣電池供電之能源短缺問題，而電源傳送效率及穩定性亦是系統效能的重要因素。系統由傳送線圈，可攜式控制盒，magnetic core, 接收線圈組成，結構示意圖如下。電源由體外裝置以無線傳輸供應到膠囊內視鏡。內視鏡內則為感應線圈。PWT 裝置外觀及使用時穿戴於身上如下圖。目前用於動物(豬)實驗中。



(6). Prof. Zhihua Yu, 中國上海 Geriatric Institute of Chinese Medicine [Study of amyloid- $\beta$  peptide functional brain networks in AD, MCI and HC] 文章已發表於 *Bio-Medical Materials and Engineering* 26 (2015) S2197–S2205。圖形理論分析應用於 Carbon 11-labeled Pittsburgh compound B 正子斷層掃描 ( $^{11}\text{C}$  PiB-PET) data 研究比較健康受試者、中度認知障礙及阿茲海默症患者的腦部 A $\beta$ 功能。結果為網絡局部叢集在中度認知障礙及阿茲海默症患者都較健康者高。且有 4 個潛在的 A $\beta$ 毒性寡合物：即 Frontal Sup Medial L、Parietal Inf L、Frontal Med Orb R and Parietal Inf R，這 4 個變異區即對應於臨床醫師斷 AD 的重要依據。如下圖：

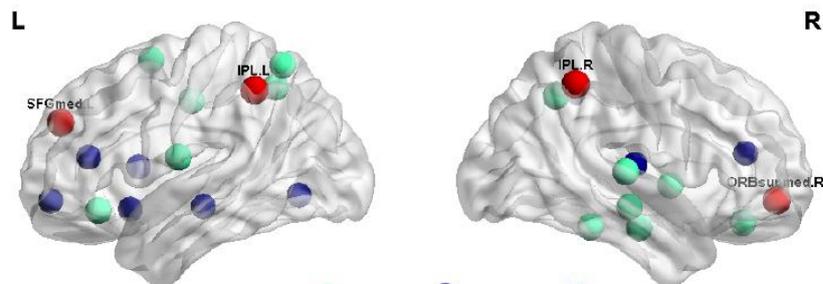


Fig. 3. Results of related alterations in hub regions. ● AD>HC; ● MCI>HC; ● AD&MCI>HC. The results were visualized by *BrainNet Viewer*.



圖 5 部分台灣參加 ICBE2015 研討會人員合照 (左起: 蔣獻文、潘醫師、陳志成、潘榕光、陳健懿及筆者)



圖 6 ICBEB2015 研討會人員合照



圖 7. 壁報論文發表會場

### 三、心得

- (一). 本次生醫工程、材料與技術國際會議相關技術領域涵括廣泛，由醫學影像類的 超音波, PET, SPECT, MRI, Xray, 雷射與螢光等輻射源、電腦運算應用於影像處理技術精進、化學物質製備技術及生醫應用、奈米材料及相關技術。而本所的輻射生醫應用研究則為其中的部分。因此有些論文發表其背景知識對我而言艱澀陌生，而部分研究較為認同且易於接受。但也因而吸收更廣泛的知識，由獲得關鍵字再自行蒐尋文獻進而了解陌生領域，有利於未來生醫應用研究觸類旁通、借用其它單位既有技術解決困難。也藉此機會與核醫界之外原本較少接觸的機構與人員有相認識的機會，促進外界對本所核醫領域應用的了解，增益本所在國際生醫應用領域知名度。對個人而言，能對國際人士說明研究成果並獲得肯定，更增加自信心。
- (二). 奈米粒子在生醫材料應用如金、二氧化鈦、或磁性氧化鐵等奈米微粒在本所及國內部分學者已有相當研究。而碳-60 等巴克球類或奈米碳管類材料也有改質技術及生醫材料產業或研究之不同應用。這些材料發展歷史較久，而反觀 2004 年發現、2010 年獲諾貝爾物理獎的石墨烯新材料，應用方向已從熟知的導電材料發展電子產業之外，其改質與應用於醫學領域相對而言仍屬新穎題材，搜尋文獻亦發現已有許多論文探討，可能是未來可發展的方向。
- (三). 本研討會歷年在大陸不同城市舉辦，此為第四屆，自 2012 年起每年依次在澳門，武漢，北京召開。大會與 IOS 國際期刊出版社合作，發表論文全文或摘要都在旗下期刊 **Bio-medical Materials and Engineering**(後來視論文屬性增加 **Human Vaccines & Immunotherapeutics**、**Basic & Clinical Pharmacology & Toxicology**、**Biomedical Signal Processing and Control** 等共四期刊)登出並可由網路檢索取得。可增加被國際研究人士搜尋參考的機會。如果以全論文型式發表，則同時刊登於雜誌專刊。且雜誌影響指數尚佳，是不錯的成果發表場合。

			
<p>Bio-medical Materials and Engineering (IF:1.09)</p>	<p>Human Vacines &amp; Immunotherapeutics (IF: 2.37)</p>	<p>Basic &amp; Clinical Pharmacology &amp; Toxicology (IF: 2.34)</p>	<p>Biomedical Signal Processing and Control (IF: 1.42)</p>

## 四、建議事項

(一) 「生物醫學工程與生物技術國際學術會議」研討會主題幾乎含括生物醫學基礎與應用各領域，與會者專長廣泛，是良好的科技整合交流應用的平台，提供原本少有接觸的各專長學者共聚激盪產生新構想的機會。但由另一角度思考，則有廣泛而失焦的缺點，此實為一體兩面難以兼顧。反觀本所進行中的各項生物醫學相關研發計畫的工作內容：應用加速器研製同位素及同位素應用、阿茲海默症診斷造影劑研發、電腦運算篩選藥效基團適當候選藥物、癌症診斷性核醫藥物及治療性標靶藥物、核醫藥物造影劑配位子 **Linker** 合成與藥物分析、前瞻分子影像診斷醫療器材技術開發、肝癌治療用核醫藥物等研究，均與輻射物質及儀器的醫學應用相關，甚至未來可能擴大往非輻射應用領域涉獵，與所外單位如中研院、工研院或生技中心等機構競爭，擴大與延伸研究領域應是未來必然趨勢，本所長官近來也積極鼓勵開拓新研究方向。建議本所研究人員應往既有熟知領域之外探索，以免畫地自限而喪失可能的機會。因此核醫藥物研究除參加核醫藥物治療及分子影像類研討會之外，可考慮嘗試跨出不同領域，例如本研討會，伸出觸角探索有點陌生的資訊，也讓外界更多領域、專長學者認識本所，啟動更多可能機會。

(二) 本次研討會首次獲悉石墨烯奈米材料改質及生醫應用，個人深感興趣，目前在本所應尚未開始進行相關工作。未來在本所研究工作中將持續關注、收集文獻並思考可以切入著力的題目。也建議本所同仁從各種專長角度考量石墨烯奈米材料可能題目或組成分工合作團隊。

(三) 本所分子影像診斷藥物開發除具輻射性質的正子及單光子輻射標誌藥物，磁共振影像(MRI)藥物也積極研發。本次邀請演講的 Case Western Reserve University 呂政榮教授在 MRI 藥物及多功能藥物輸送系統以傳送治療的 siRNA，對轉移性乳癌的研究都有所成。若呂教授有機會訪台，建議邀請蒞所演講，對本所相關研

究應有相當助益。

(四) 生技醫藥技術與產業的發展，關乎國人生命健康與生活品質，在國人高齡化社會來臨之際其重要性更甚以往。政府與國人對健康相關的投資與支出必定逐年快速成長。觀察國內每年辦理的生技月展，可發現參展廠商踴躍，但展示內容之技術層次偏低且多所重複，例如健康食品類、化妝品類等。建議國內應更多辦理國際生醫技術工程等相關論壇，引導產業投資技術層次更高的生醫技術與產品。而我輩等提早構思與因應研究計畫是乘勢而起的關鍵。

(五) 明年第五屆生物醫學工程與生物技術國際學術會議，ICBEB 2016 將於 2016 年 8 月 8 日至 11 日在杭州召開。相關資訊已公告網頁 <http://cn.icbeb.org/>。

## 五、附 件

### 附件一 議程

**Tuesday Aug. 18, 2015**

Time	Activity	Location
08:00-19:00	Registration	Lobby of Mecure Shanghai Royalton( Royalton Hotel)

Notes: Please take Participating Card for the venue and Tour Card for the tour.

**Wednesday Morning, Aug. 19**

Time	Activity	Location: 5 <sup>th</sup> floor, Crown Hall
08:30-08:40	Opening Ceremony	
08:40-09:25	Keynote Speech 1: An LMS Algorithm for Characterization of BioSignal Shape <i>Dr. Edward J. Ciaccio</i>	
09:25-10:10	Keynote Speech 2: Computer-Aided Diagnosis of Myocardial Infarction Using Ultrasound Images with Second-Order Statistics, DWT and HOS Methods: A Comparative Study <i>Dr. Ng Yin Kwee</i>	
10:10-10:30	Pose for a Group Photo and Coffee Break	
10:30-11:15	Keynote Speech 3: Surgical Imaging, Biophotonics and Endoscopy <i>Dr. Daniel Elson</i>	
11:15-12:00	Keynote Speech 4: Early Detection and Treatment of Metastatic Breast Cancer <i>Prof. Zheng-Rong Lu</i>	

**Wednesday Noon, Aug. 19**

12:30-13:30	Buffet Lunch	Location: 2 <sup>nd</sup> floor, Hong Kong Hall
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**Wednesday Afternoon, Aug. 19**

Time	Poster Presentation	Location
14:00-14:45	Keynote Speech 5: The Importance of Scientific Journals for Advancement in Biomedicine <i>Prof. David De Jong</i>	5 <sup>th</sup> floor, Crown Hall
14:45-15:00	Coffee Break	3 <sup>rd</sup> floor, Royal Hall I
15:00-16:00	Poster 1: Biomedical Engineering	3 <sup>rd</sup> floor, Royal Hall I
	Poster 2: Biomedical Imaging & Signal Processing	
16:00-17:00	Poster 3: Biomaterial	
	Poster 4: Biomechanical Engineering	

**Wednesday Evening, Aug. 19**

17:00-17:45	Buffet Dinner	Location: Oasis Tower Hotel
18:00-21:00	Gathering at the lobby of Oasis Tower Hotel at 17:45 and going for a trip to the Bund and Huangpu River Cruises	

**Thursday Morning, Aug. 20**

Time	Oral Presentation	Location
08:00-12:00	Oral 1: Biomedical Engineering	4 <sup>th</sup> floor, Hugo Hall
	Oral 2: Biomedical Imaging & Signal Processing (1)	3 <sup>rd</sup> floor, Royal Hall II
	Oral 3: Biomaterial	4 <sup>th</sup> floor, Zola Hall

**Thursday Noon, Aug. 20**

12:00-13:00	Buffet Lunch	Location: 2 <sup>nd</sup> floor, Hong Kong Hall
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**Thursday Afternoon, Aug. 20**

Time	Oral Presentation	Location
14:00-17:30	Oral 4: Biomechanical Engineering	4 <sup>th</sup> floor, Hugo Hall
	Oral 5: Biomedical Imaging & Signal Processing (2)	3 <sup>rd</sup> floor, Royal Hall II

**Thursday Evening, Aug. 20**

18:00-19:30	Awarding Dinner	Location: Oasis Tower Hotel
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## **Forced degradation characterization of H<sub>3</sub>MN-16ET using liquid chromatography-tandem mass spectrometry**

P. C. WANG<sup>1</sup>, W. H. CHEN<sup>1\*</sup>, T. Y. LUO<sup>2</sup>, Y. C. HSIAO<sup>1</sup> and Y. CHANG<sup>1</sup>

<sup>1</sup>*Chemistry Division, Institute of Nuclear Energy Research, Taoyuan, Taiwan*

<sup>2</sup>*Isotope Application Division, Institute of Nuclear Energy Research, Taoyuan, Taiwan*

*\*Corresponding author; E-mail:whchen@iner.gov.tw, Tel.:886-3-4711400#5012*

### **Aims:**

H<sub>3</sub>MN-16ET, a new ligand with N<sub>2</sub>S<sub>2</sub> tetra-dentate and hexadecyl carboxylate ethyl ester side chain, was labeled with <sup>188</sup>Re to form <sup>188</sup>Re-MN-16ET which is under preclinical evaluation for hepatoma radio-therapy. The aim of this study is to investigate the forced degradation characteristic of H<sub>3</sub>MN-16ET under stressed conditions including acidic / alkaline, oxidation, UV and thermal exposure.

### **Method:**

H<sub>3</sub>MN-16ET was dissolved in methanol and treated with five kind of stressed conditions including basic hydrolysis (0.1 M NaOH), acidic hydrolysis (0.1 M HCl), oxidation (3% H<sub>2</sub>O<sub>2</sub>), photolysis (UV, 254 nm) and thermal (80°C) conditions respectively. The samples were taken at 0, 1, 2, 4, 8, 16 and 24 hours and determined the degradation rate and products identity of H<sub>3</sub>MN-16ET using liquid chromatography coupled with tandem mass spectrometry methodology (LC-UVD-MS/MS).

### **Results:**

The results indicated that H<sub>3</sub>MN-16ET was hydrolyzed easily in basic / acidic after 1 and 2 h, respectively. Also, H<sub>3</sub>MN-16ET was almost degraded after 24 h under UV radiation. It was degraded 45% after 24 h with thermal condition. However, the ligand was relative stable under oxidation condition, without degraded product was found within 24 h. The tandem mass spectra of spoiled products from H<sub>3</sub>MN-16ET stressed conditions were examined and proposed the possible chemical structures.

### **Conclusions:**

From the above study, we found that H<sub>3</sub>MN-16ET cannot stand for acidic / basic hydrolyzed and it will be decomposed under UV and heat exposure. But H<sub>3</sub>MN-16ET might be durable for oxidative potential. It is meaningful to find out the deteriorated causes and pathways of H<sub>3</sub>MN-16ET about shelf life, storage conditions and preparation quality for pharmacy.

The 4<sup>th</sup> International Conference on  
Biomedical Engineering and Biotechnology (ICBEB2015)

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**ACCEPTANCE NOTIFICATION**

June 1, 2015

Congratulations! We are extremely glad to inform you that your contribution:

PAPER ID: CBB2108

**ABSTRACT: Forced degradation characterization of H3MN-16ET using liquid chromatography-tandem mass spectrometry**

has been accepted by ICBEB2015 as conference abstract and will be published in a supplement issue of *Basic & Clinical Pharmacology & Toxicology*, which is indexed both by SCI and SCI Expanded. We are grateful for your contribution to ICBEB2015. We also hope that you will contribute your excellent work to future ICBEB conferences.

For more information, please visit our website: [www.icbeb.org](http://www.icbeb.org)

If you have any question, please feel free to contact us.

We are looking forward to meeting you in Shanghai, China.

Best regards,

ICBEB 2015 Organizing Committee





The 4th International Conference on Biomedical Engineering and Biotechnology (ICBEB2015)  
August 18th - 21st, 2015, Shanghai, China



## Forced degradation characterization of H<sub>3</sub>MN-16ET using liquid chromatography-tandem mass spectrometry

P. C. WANG<sup>1</sup>, W. H. CHEN<sup>1\*</sup>, T. Y. LUO<sup>2</sup>, Y. C. HSIAO<sup>1</sup> and Y. CHANG<sup>1</sup>

<sup>1</sup>Chemistry Division, Institute of Nuclear Energy Research, Taoyuan, Taiwan

<sup>2</sup>Isotope Application Division, Institute of Nuclear Energy Research, Taoyuan, Taiwan

\*Corresponding author, E-mail: whchen@iner.gov.tw, Tel.: 886-3-4711400#5012

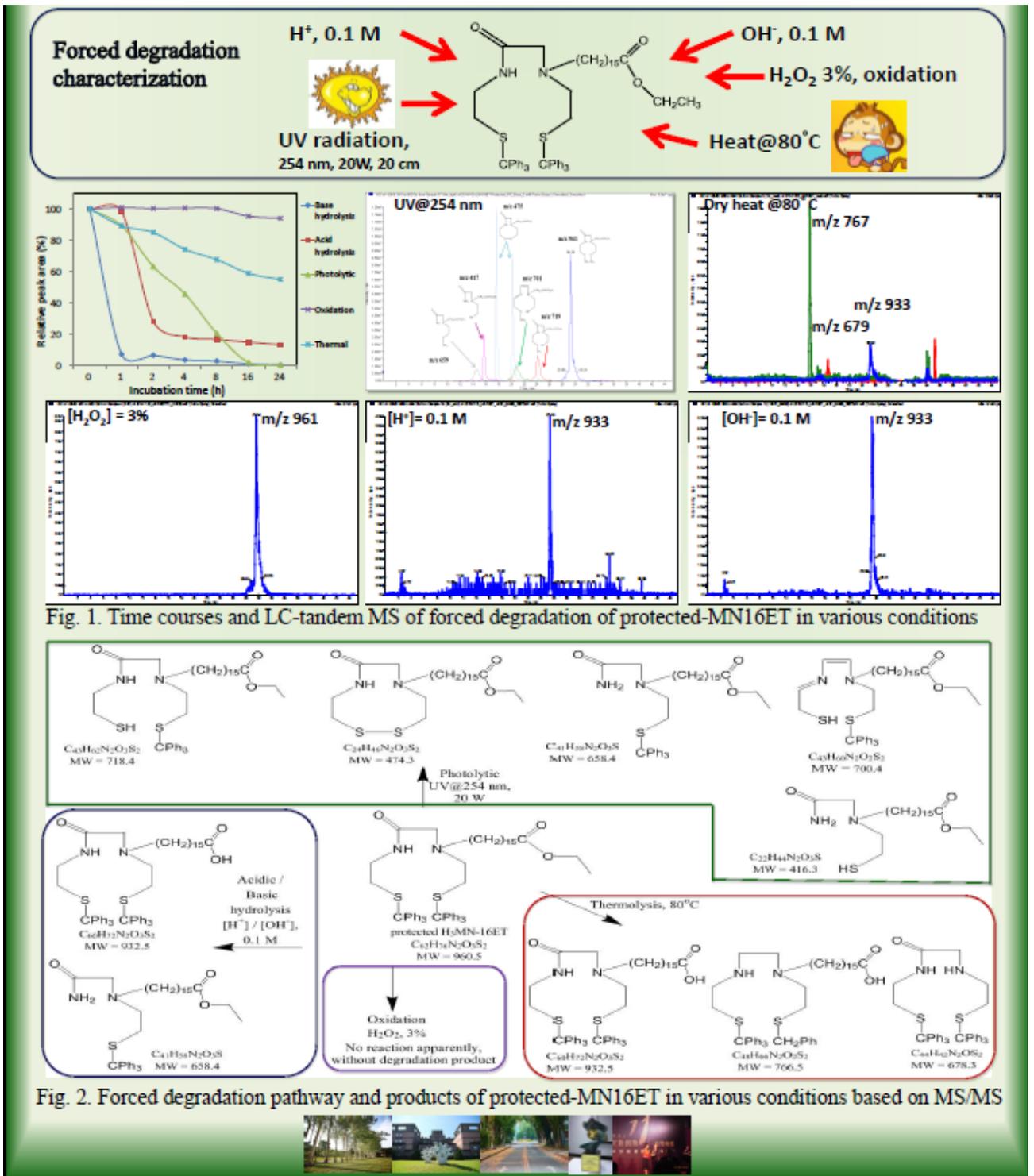
**Aims:** H<sub>3</sub>MN-16ET, a new ligand with N<sub>2</sub>S<sub>2</sub> tetra-dentate and hexadecyl carboxylate ethyl ester side chain, was labeled with <sup>188</sup>Re to form <sup>188</sup>Re-MN-16ET which is under preclinical evaluation for hepatoma radio-therapy. The aim of this study is to investigate the forced degradation characteristic of H<sub>3</sub>MN-16ET under stressed conditions including acidic / alkaline, oxidation, UV and thermal exposure.

**Method:** H<sub>3</sub>MN-16ET was dissolved in methanol and treated with five kind of stressed conditions including basic hydrolysis (0.1 M NaOH), acidic hydrolysis (0.1 M HCl), oxidation (3% H<sub>2</sub>O<sub>2</sub>), photolysis (UV, 254 nm) and thermal (80°C) conditions respectively. The samples were taken at 0, 1, 2, 4, 8, 16 and 24 hours and determined the degradation rate and products identity of H<sub>3</sub>MN-16ET using liquid chromatography coupled with tandem mass spectrometry methodology (LC-UVD-MS/MS).

**Results:** The results indicated that H<sub>3</sub>MN-16ET was hydrolyzed easily in basic / acidic after 1 and 2 h, respectively. Also, H<sub>3</sub>MN-16ET was almost degraded after 24 h under UV radiation. It was degraded 45% after 24 h with thermal condition. However, the ligand was relative stable under oxidation condition, without degraded product was found within 24 h. The tandem mass spectra of spoiled products from H<sub>3</sub>MN-16ET stressed conditions were examined and proposed the possible chemical structures.

**Conclusions:** From the above study, we found that H<sub>3</sub>MN-16ET cannot stand for acidic / basic hydrolyzed and it will be decomposed under UV and heat exposure. But H<sub>3</sub>MN-16ET might be durable for oxidative potential. It is meaningful to find out the deteriorated causes and pathways of H<sub>3</sub>MN-16ET about shelf life, storage conditions and preparation quality for pharmacy.





附件四

口頭報告論文發表題目目錄

**Oral Session\_1 Biomedical Engineering**

Session chair: Alexander Spector

Time: 08:00-12:00

Location: 4<sup>th</sup> floor, Hugo Hall

Time	Paper ID	Paper Title	Author
08:00-08:15	CBB1164	Temporal integration reflected by frequency following response in auditory brainstem	Qin Xu
08:15-08:30	CBB1459	A new method to accurately assess post-laser-surgery refractive changes with the intrinsic corneal power changes	Yongji Liu
08:30-08:45	CBB1536	A Method to Optimize the Socket Design of a Lower Extremity Prosthesis	Kivilcim Ersoy
08:45-09:00	CBB1617	Mental workload prediction based on attentional resource allocation and information processing	Xiao Xu
09:00-09:15	CBB1622	A Method of Extracting Disease-Related microRNAs Through the Propagation Algorithm Using the Environmental Factor Based Global miRNA Network	Jihwan Ha
09:15-09:30	CBB1755	Effect of Mechanical Cues on Adipose-Derived Stem Cell Myogenesis: Insight from a Kinetic Model	Alexander Spector
09:30-09:45	CBB1852	A portable wireless power transmission system for video capsule endoscopes	Gang Liu
09:45-10:00	CBB2026	Study of amyloid- $\beta$ peptide functional brain networks in AD, MCI and HC	Huoqiang Duan
10:00-10:15	CBB2029	A Computational Model of Platelet Flow in a Carotid Artery Bifurcation	Guojie Li
10:30-10:45	CBB2118	The Temperature Field Simulation and Phantom Validation of a Two-armed Spiral Antenna for Microwave	Lingze Zhang
10:45-11:00	CBB2158	Design and Compatibility Evaluation of MRI-Guided Needle Insertion System	Peng Zhang
11:00-11:15	CBB2305	Analysis of Protein Complex Associated to Actin Homolog MreB in Helicobacter pylori	Xianwu Guo
11:15-11:30	CBB2373	Antipyretic mechanism of cinnamaldehyde involved in regulation of TRPV1 channel in DRG neurons	Feng Sui
11:30-11:45	ICBE2169	Investigating the modulation of brain activity associated with handgrip force and fatigue	Liu Cao
11:45-12:00	ICBE2204	Studying Frequency Processing of the Brain to Enhance Long-term Memory, Develop a Human Brain Protocol	Wernher Friedrich

## Oral Session\_2 Biomedical Imaging & Signal Processing (1)

Session chair: Lung Kwang Pan

Time: 08:00-12:00

Location: 3<sup>rd</sup> floor, Royal Hall II

Time	Paper ID	Paper Title	Author
08:00-08:15	CBB1066	Binary particle swarm optimization for frequency band selection in motor imagery based brain-computer interfaces	Qingguo Wei
08:15-08:30	CBB1079	EEG-based research on brain functional networks in cognition	Li Zhang
08:30-08:45	CBB1171	An analysis of pulse wave signals during Visual Display Terminal operations	Yang Lu
08:45-09:00	CBB1292	Automatic detection of regions of interest in breast ultrasound images based on local phase information	Xin Wang
09:00-09:15	CBB1325	Scattered radiation doses absorbed by technicians at different distances from X-ray exposure: Experiments on prosthesis	Hsien-Wen Chiang
09:15-09:30	CBB1369	Automatic segmentation of adrenal tumor in CT images based on sparse representation	Hanchao Chai
09:30-09:45	CBB1401	Optimization of the imaging quality of 64-slice CT acquisition protocol using Taguchi analysis: A phantom study	Lung Kwang Pan
09:45-10:00	CBB1456	Pathological brain detection based on wavelet entropy and Hu moment invariants	Yudong Zhang
10:00-10:15	CBB1467	In vivo evaluating skin doses for lung cancer patients undergoing Volumetric Modulated Arc Therapy treatment	Chien Yi Chen
10:30-10:45	CBB1468	Quantitative evaluation of contrast-induced-nephropathy in vascular post-angiography patients: Feasibility study of a semi-empirical model	Lung Fa Pan
10:45-11:00	CBB1507	Ultrasound Imaging and Pulsed Wave Doppler Stimulus Fetal Reflex Action Test	Samreen Amir
11:00-11:15	CBB1531	Detection of Perlegr-Huet anomaly based on augmented Fast Marching Method and Speeded Up Robust Features	Shaobao Yang
11:15-11:30	CBB1533	Assessment of the Effectiveness of DWI-ASPECTS in Predicting the Functional Outcomes of Cerebral Infarction Patients after Thrombolysis	Liang Jiang
11:30-11:45	CBB1576	A CT reconstruction approach from sparse projection with adaptive-weighted diagonal total-variation in biomedical application	Luzhen Deng
11:45-12:00	CBB2256	Assessment of Cardiac Time Intervals by Wavelet Transform of the Impedance Cardiogram	Rodion Stepanov

### Oral Session\_3 Biomaterial

Session chair: Hong Qiu

Time: 08:00-12:00

Location: 4<sup>th</sup> floor, Zola Hall

Time	Paper ID	Paper Title	Author
08:00-08:15	CBB1123	Antibacterial, anti-inflammatory, and antioxidant effects of Yinzhihuang injection	Hong Qiu
08:15-08:30	CBB1546	Color difference threshold determination for acrylic denture base resins	Jiabao Ren
08:30-08:45	CBB1560	Analysis of nervous fiber, muscle, and blood vessels using their ultraviolet near infrared reflectance characteristics	Kadir Tufan
08:45-09:00	CBB1939	Evaluation of the micro-shear bond strength of four adhesive systems to dentin with and without adhesive area limitation	Yuan Chai
09:00-09:15	CBB1947	A comparison study on the flexural strength and compressive strength of four resin-modified luting glass ionomer cements	Yuan Li
09:15-09:30	CBB2062	Strength degradation and lifetime prediction of dental zirconia ceramics under cyclic normal loading	Wanzhong Li
09:30-09:45	CBB2077	Increased sensitivity of 3D-Well enzyme-linked immunosorbent assay (ELISA) for infectious disease detection using 3D-printing fabrication technology	Harpal Singh
09:45-10:00	CBB2368	Hepatoprotective effect of Cinnamon on cholesterol induced Fatty changes in albino rats	Zahid Iqbal
10:00-10:15	CBB2415	Biopolymer-graphene nanocomposite microneedles for transdermal	Biqiong Chen
10:30-10:45	CBB2423	Biodegradable nanoporous microspheres for controlled drug delivery system	Ildoo Chung

### Oral Session\_4 Biomechanical Engineering

Session chair: Bin Chen

Time: 14:00-17:30

Location: 4<sup>th</sup> floor, Hugo Hall

Time	Paper ID	Paper Title	Author
14:00-14:30	CBB1942	Computational hemodynamics of the portal vein hypertension in hepatic cirrhosis patients	Bin Chen
14:30-14:45	CBB1144	Research of gestational diabetes mellitus risk evaluation method	Zhenyu Chi
14:45-15:00	CBB1258	Improved walking ability with wearable robot-assisted training in patients suffering chronic stroke	Lifang Li
15:00-15:15	CBB1302	Application of uniform design to improve dental implant system	Yung-Chang Cheng
15:15-15:30	CBB1462	Numerical analysis of the effect of side holes of a double J stent on flow rate and pattern	Young Ho Choi
15:45-16:00	CBB1565	Design of a biped robot actuated by pneumatic artificial muscles	Yixiang Liu

16:00-16:15	CBB1604	Hemodynamics investigation for a giant aneurysm treated by a flow diverter	Shengzhang Wang
16:15-16:30	CBB1728	4D Model of Hemodynamics in the Abdominal Aorta	Ireneusz Zbicinski
16:30-16:45	CBB1956	Experimental analysis of robot-assisted needle insertion into porcine liver	Wendong Wang
16:45-17:00	ICBE1468	Research on seamless development of surgical instruments based on biological mechanisms using CAD and 3D printer	Ikuo Yamamoto
17:00-17:15	ICBE2320	Design improvement and dynamic finite element analysis of novel ITI dental implant under dynamic chewing loads	Yung-Chang Cheng

### Oral Session\_5 Biomedical Imaging & Signal Processing (2)

Session chair: Chunliang Wang

Time: 14:00-17:30

Location: 3<sup>rd</sup> floor, Royal Hall II

Time	Paper ID	Paper Title	Author
14:00-14:15	CBB1672	The application of EMD in activity recognition based on a single triaxial accelerometer	Mengjia Liao
14:15-14:30	CBB1715	Automatic localization of macula fovea based on wavelet transformation and gray contours	Xinpeng Zhang
14:30-14:45	CBB1730	Computer-aided detection of lung nodules using outer surface features	Önder Demir
14:45-15:00	CBB1741	An Integrated Approach Utilising Imaging and Computer Aided Design of MR images for Customized Medical Knee Implants Production	Ahmad Majdi Abdul Rani
15:00-15:15	CBB1744	EEG functional network properties related to visually induced unrecognized spatial disorientation	Yuanyuan Chen

15:15-15:30	CBB1805	Simultaneous measurement of multiple scattering coefficient and scattering anisotropy factor in dental demineralization	Meng-Chun Kao
15:45-16:00	CBB1898	Enhance contrast in PCA based beamformers using smoothing kernel	Saeid Aliabadi
16:00-16:15	CBB1924	Preliminary Research on Abnormal Brain Detection by Wavelet-Energy and Quantum-Behaved PSO	Shuihua Wang
16:15-16:30	CBB1967	Electroencephalogram assessment of mental fatigue in visual search	Xiaoli Fan
16:30-16:45	CBB2025	A novel A $\beta$ segmentation algorithm based on 3D Lattice Boltzman Method	Xinghui Shu
16:45-17:00	CBB2234	A Modified Fuzzy C-Means Method for Segmenting MR Images Using Non-local Information	Yuan Feng
17:00-17:15	CBB2297	Real-time Interactive 3D Tumor Segmentation Using a Fast Level-set Algorithm	Chunliang Wang
17:15-17:30	CBB2432	Electroencephalography (EEG) for Detecting Acute Ischemic Stroke	Sastra Kusuma Wljaya
17:30-17:45	CBB2131	Analysis of the effect of the secondary Procedure in Magneto-Acoustic Tomography and Magneto-Acousto-Electrical Tomography	Zhishen Sun