出國報告（出國類別：進修）

美國耶魯大學核子醫學科進修報告

服務機關：臺大癌醫中心分院
姓名職稱：柯冠吟主治醫師
派赴國家/地區：美國康乃狄克州
出國期間：113 年 8 月 1 日至 114 年 1 月 31 日
報告日期：114 年 2 月 7 日

摘要

核醫放射性核種治療是當今醫學領域中一項日益受到關注的精準治療之一，核醫藥物治療之前、後各有其相對應的不同核醫影像檢查。另，影像診斷與分析、核醫治療介入時機、與治療劑量評估，都是重要的臨床議題且具研究價值。職於 105 年升任核醫主治醫師，於 110 年起擔任核醫主任，渴望能透過進修接觸國外頂尖醫院，了解美國在核醫新興檢查與治療上的最新進展。有幸在院方、師長及耶魯大學醫學院陳明楷教授的大力支持下，以訪問學者 (Visiting Scholar) 身份造訪耶魯大學醫學院以及附設醫院。此次經驗不僅拓展專業知識，更豐富人生經驗，期盼在未來能與耶魯大學建立更加深入的合作與交流，為核醫學領域的發展持續努力。

目次

目的

近幾年，核子醫學放射性核種治療特別是使用在神經內分泌腫瘤的 Lu-177 Dotatate (Lutathera)治療、使用在攝護腺癌的 Lu-177 PSMA (Pluvicto) 治療是當今醫學領域中日益受到關注的精準治療之一，隨著核醫放射性標靶治療的興起，許多重要的臨床議題逐漸浮現，例如：核醫治療前以及治療後相對應的不同核醫影像檢查分析、核醫治療介入時機、治療劑量評估以及輻射防護議題皆與病人的治療成效與預後息息相關。這些治療是透過放射性同位素的應用，能夠精準鎖定腫瘤細胞，大幅度地降低對周圍健康組織的傷害，並提升療效。由於這些治療的成功實施依賴醫師具備高度專業的知識與技術，因此，深化核子醫學治療的研究和專業進修是當前的重要需求。

過程

職於臺大核子醫學部接受完整核醫學訓練之後，於 105年升任主治醫師，於110年擔任核醫主任，參與新型同位素治療的設置、治療計畫與臨床照護，希望透過出國進修，深入了解國外優秀大學附設醫院在核醫影像檢查與新興治療方面的最新發展，以更提升臨床知識與經驗，並將導入最新的治療技術及觀念，期許此進修能提供患者更優質的醫療服務。

2022 年邀請國外學者：耶魯醫學院核子醫學科陳明楷教授，到臺大演講訪談之後，開始與教授聯繫接洽與密切交流，並在 113 年能有幸以訪問學者(Visiting Scholar)身份造訪耶魯大學，報到與受訓步驟概述如下：於耶魯大學 Office of International Students & Scholars (OISS) connect 系統上創建帳號，提交辦理簽證所需文件以及上傳各項個人資料、學術經歷等文件；登入美國聯邦 Student and Exchange Visitor Information System (SEVIS) 網頁完成 I-901 文件與繳費並且預約美國在臺協會(AIT)面試；耶魯大學校方創立 Yale Net ID 與 email，於 Homebase 完成線上職前訓練；於 Workday 完成填寫有關個人資料、可能會涉及的研究項目、薪資與稅務等相關內容與課程．

<u>到職後的第一週</u>

至美國出入境管理網站下載入境證明 I -94，啟動 SEVIS。

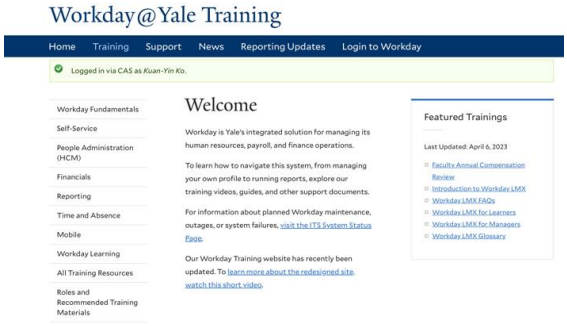
(1) 登入OISS 系統提出新進員工到職申請。

(2) 完成線上 HOMEBASE 所分派之教育課程，包括病人安全、實驗室安全、性騷擾防治、資訊安全等。

(3) 攜帶護照等文件辦理耶魯識別證，以便通行校園與醫院。

(4) 開立銀行帳戶，上 Workday 登錄相關資訊並完成填寫美國稅務相關表單。

(5) 租房簽約、租車與辦理美國電信門號



<u>學術活動</u>

參與癌症團隊會議

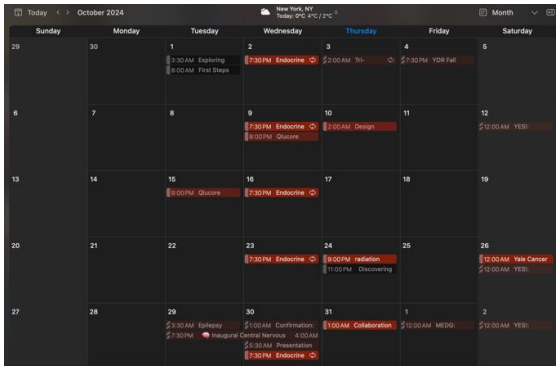
開會時間各科別皆不同，自從COVID-19 疫情後，各團隊大多使用 Zoom 平台，邀請職類團隊成員，開會討論時間約在一或一個半小時之間，Schedule as follows:

W1 12:00 PM GU, 3:30 PM thoracic tumor board, 4:00 PM GI

W2 8:30 AM Lymphoma

W3 7:30 AM Endocrine

W4 7:30 AM Melanoma, 4:00 PM Pediatric tumor



Yale SCHOOL OF MEDICINE

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Transcript Period 1/1/2011 to 1/20/2025 | **Created On:** 1/20/2025

Transcript Credit Summary:

AMA PRA Category 1 Credits™: 78.00 Credits
General Attendance: 1.00 Credits
Non-Physician Attendance: 14.75 Credits

Credit Type: *AMA PRA Category 1 Credits™* **Total:** 78.00

ID	Session	Activity Name/Date	Activity Format	Credits	Claim Date
43766	44514-43766	Pediatric Tumor Board, July 4, 2024 - June 26, 2025	Live Activity		
	44514-43766	Pediatric Tumor Board - 9/5/2024, September 5, 2024		1.00	9/5/2024
	44515-43766	Pediatric Tumor Board - 9/12/2024, September 12, 2024		1.00	9/12/2024
	44520-43766	Pediatric Tumor Board - 10/17/2024, October 17, 2024		1.00	10/17/2024
	44524-43766	Pediatric Tumor Board - 11/14/2024, November 14, 2024		1.00	11/14/2024
43737	43991-43737	Thoracic Tumor Board, July 8, 2024 - June 30, 2025	Live Activity		
	43991-43737	Thoracic Tumor Board - 9/9/2024, September 9, 2024		1.50	9/9/2024
	43992-43737	Thoracic Tumor Board - 9/16/2024, September 16, 2024		1.50	9/16/2024
	43993-43737	Thoracic Tumor Board - 9/23/2024, September 23, 2024		1.50	9/23/2024
	43994-43737	Thoracic Tumor Board - 9/30/2024, September 30, 2024		1.50	9/30/2024
	43995-43737	Thoracic Tumor Board - 10/7/2024, October 7, 2024		1.50	10/7/2024
	43996-43737	Thoracic Tumor Board - 10/14/2024, October 14, 2024		1.50	10/14/2024
	43997-43737	Thoracic Tumor Board - 10/21/2024, October 21, 2024		1.50	10/21/2024
	43998-43737	Thoracic Tumor Board - 10/28/2024, October 28, 2024		1.50	10/28/2024
	44001-43737	Thoracic Tumor Board - 11/18/2024, November 18, 2024		1.50	11/18/2024
	44002-43737	Thoracic Tumor Board - 11/25/2024, November 25, 2024		1.50	11/25/2024
	44003-43737	Thoracic Tumor Board - 12/2/2024, December 2, 2024		1.50	12/2/2024
43754	44203-43754	Gastrointestinal Tumor Board, July 1, 2024 - June 30, 2025	Live Activity		
	44203-43754	Gastrointestinal Tumor Board - 9/9/2024, September 9, 2024		1.50	9/9/2024
	44207-43754	Gastrointestinal Tumor Board - 10/7/2024, October 7, 2024		1.50	10/7/2024

Yale Continuing Medical Education is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The activities listed have been approved for *AMA PRA Category I Credits ™*

Total: **78.00**

cme@yale.edu

Notes: The process is similar to that of our hospital. Physicians are encouraged to freely express their opinions, and for each case, the chairperson summarizes and establishes a consensus. Additionally, educational topics are provided to support the learning and development of junior clinicians and trainees.

參加醫學院課程

核醫學藥物製藥與藥物動力學課程，由研究學者進行小班演講與討論，講題每週不同，課程表與授課狀況如下圖

Pharmacokinetics & Pharmacodynamics in Neuropharmacology

2:00 pm – 3:15 pm on Tuesday in SHM B222
2:15 pm – 3:30 pm on Friday in SHM B201
Course Coordinator: Jason Cai; jason.cai@yale.edu; (573) 823-0652

Instructors
Jason Cai, PhD
Richard Carson, PhD
Nicolas Guehl, PhD
Henry Huang, PhD
Songye Li, PhD
David Matuskey, MD
Adam Mecca, MD
Marc Normandin, PhD
Rajiv Radhakrishnan, MD
Istvan Szanda, PhD
Tommaso Volpi, MD/PhD
Moses Wilks, PhD

Course Overview
This course (**PHAR538**) is designed to introduce state-of-the-art imaging methods in the study of neuropharmacology. It covers topics on *Medicinal Chemistry, Pharmacology, Neuroscience* and *Advanced Molecular Imaging* and is designed for graduate students who are interested in imaging and quantitative neuropharmacology. This course features the applications of advanced imaging technologies in the preclinical and clinical neuropharmacology.
The lecturer group is comprised with leading experts in Medicinal Chemistry, Neuropharmacology and Molecular Imaging. The classroom constitutes didactic lectures and interactive discussion sections. The classroom activities facilitate students to appreciate and critically evaluate literature in neuropharmacology and prepare students to use advanced translational quantitative imaging methods in the study of systemic neuropharmacology.

Recommended Textbook/Book Chapters
Molecular Neuropharmacology, *Nestler, Hyman & Malenka, 4th edition*

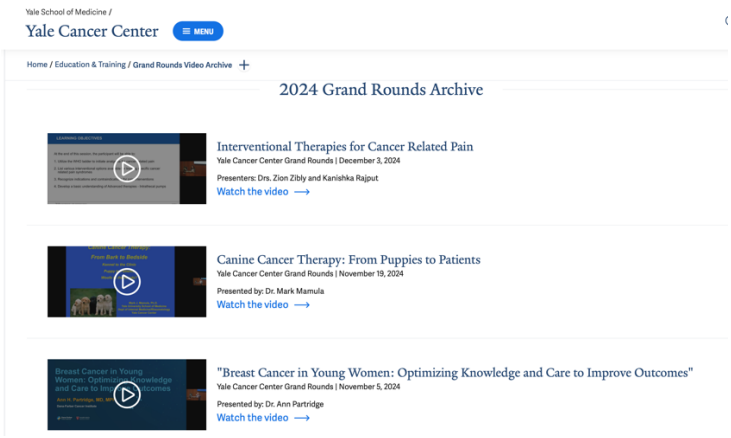
Course Schedule

Date	Subject	
Module I	**Neuropharmacology**	
9.3.2024	Course Overview	Jason Cai
9.6.2024	PET Imaging in Neuropharmacology	Jason Cai
9.10.2024	Introduction to the Central Nervous System	Nira Hernandez
9.13.2024	*BIS retreat*	
9.17.2024	Molecular Basis of PK/PD	Jason Cai
9.20.2024	***Exam 1***	
Module II	**Kinetic Modeling in PK/PD: Principles of Quantitative PET Imaging**	
9.24.2024	PET PK/PD Principles	Nicolas Guehl
9.27.2024	Compartmental models	Nicolas Guehl
10.1.2024	Linear, graphical methods	Moses Wilks/Marc
10.4.2024	Reference region-based methods	Moses Wilks
10.8.2024	Dynamic Neurotransmitter Imaging & Receptor Occupancy	Marc Normandin
10.11.2024	Imaging opioid receptors in depression	Songye Li
	October Recess (Oct 15-20)	
10.22.2024	Opportunities for kinetic modeling with ultra-high performance PET scanners	Tommaso Volpi
10.25.2024	***Exam 2***	
Module III	**Applications in Neuropharmacology**	
10.29.2024	Imaging NMDA, and glutamate systems	Rich Carson
11.1.2024	Dopaminergic and Cannabinoid systems in schizophrenia and cannabis use disorder	Rajiv Radhakrishnan
11.5.2024	Imaging Dopamine and serotonin systems in vivo	Henry Huang
11.8.2024	Alzheimer's disease	Adam Mecca
11.12.2024	Parkinson's disease, meditation, and GABA imaging	David Matuskey
11.15.2024	Developing PET tracer for neuroimaging	Henry Huang

This class focuses on the pharmacokinetics (PK) and pharmacodynamics (PD) of neuro radiopharmaceuticals, covering topics from molecular foundations and kinetic modeling to clinical applications.

Grand Runs

Yale 醫學院各科部定期有舉辦Grand Run, in-person 與 virtual並行，實體與會備有餐點可享用，若無法實體參與也可以線上參與進行討論，會後也會將Grand Run的錄影上傳導到網頁及YouTube，方便臨床忙碌的同仁事後觀看．



2024 grand rounds archive

Topic: PET/MR Molecular Imaging of Cancer

Yale Cancer Center Grand Rounds (September 17, 2024)

Presented by: Georges El Fakhri, PhD, DABR

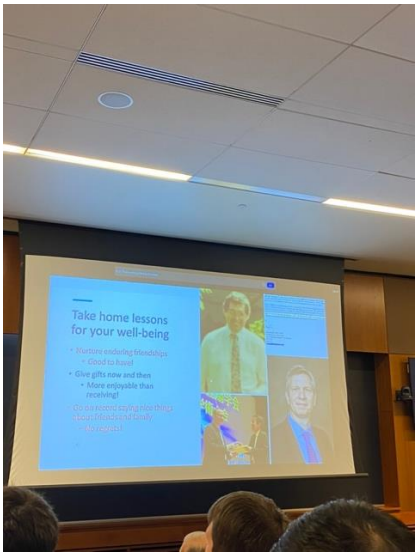
參與各項研討會及講座

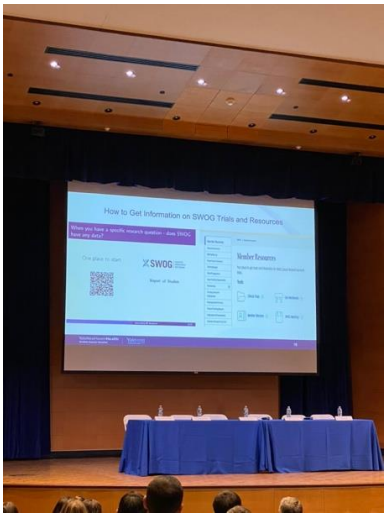
參加放射腫瘤科專家紀念講座：A lecture organized by the foundation established by the family of the late radiation oncologist Dr. Roy Decker. This session introduced the history of radiation oncology and the life and works of Dr. Decker.

臨床試驗中心講座：An event hosted by Yale's Clinical Trial Center, featuring presentations from principal investigators and team members involved in various clinical trials. One of the key presentations was delivered by the SWOG (Southwest Oncology Group) leader, who provided an in-depth overview of Lung-MAP, a large-scale, nationwide study involving numerous medical institutions and over ten pharmaceutical companies, focusing on new drug development and immunotherapy for lung cancer. The second part of the lecture involved participants from

various levels of clinical trials, sharing experiences on how to join, participate, and collaborate across trial teams.

參加 Radiology & Biomedical Imaging Grand Rounds Boroff-Forman Lecture Series 會議"More Care to More Veterans Than Ever Before"。探討軍人潛在暴露(Agent Orange, Burn Pit, Camp lejeune contaminated water, k2 uzbekistan radiation)與誘發疾病: The discussion also covered the passing of the PACT Act and the efforts of the Department of Veterans Affairs in actively supporting veterans affected by these exposures.

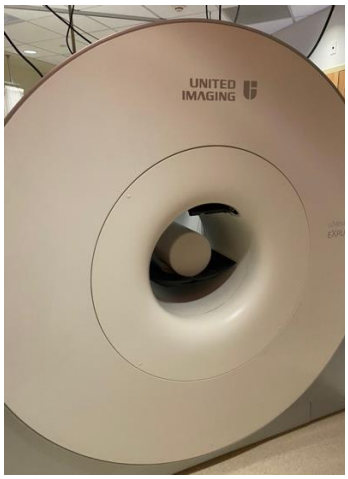




YNHH nuclear medicine AND PET center

走訪核醫治療病房、治療室、正子中心、影像閱片室及藥劑配製室，並觀摩藥物劑量測定與配製、衛教流程以及施打過程。此外，也參觀了核醫科工作站、PACS 系統與影像分析軟體。核醫科設於 Yale New Haven Hospital Smilow 大樓的二樓，同樓層設有醫師閱覽室、熱核室、影像處理工作站及多間注射室/治療室。此外，八樓有兩間化療空間，配合執行非碘治療。耶魯大學正子中心配備了專用於研究的 HRRT PET/CT（舊型）及 uNeuroExplorer PET/CT。醫師閱覽室共配置八組工作站供醫師使用，每一組工作站搭配三個醫療級螢幕、電動升降桌、機械鍵盤、語音系統(麥克風控制把手)。Using MIM, visage

software for imaging display and analysis. 臨床使用 Epic 系統，是一個可以整合病患資訊、醫囑流程、增進醫療透明化的系統．Brief impression: Interface is very easy to use and organized, incorporate every notes (including telephone medicine, research records), image, exams and orders.



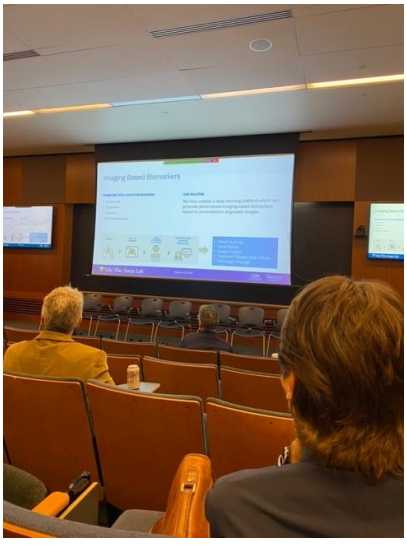

Lu-177 PRRT/RLT

治療空間地板舖設塑膠防水紙，人員進行治療前須戴上手套與鞋套，佩戴輻射佩章但皆無穿鉛衣。病患使用周邊靜脈，與 syringe pump(25 c.c./30 分鐘)，外有鉛盒提供屏蔽。注射前醫師進行衛教與簽署同意書，團隊進行 Time-out 後開始輸注，注射期間觀察注射部位與可能副作用，結束完後量測注射處劑量與一公尺劑量。待氨基酸輸注完成(四小時)後，若無顯著副作用，病患可離院．Lu-177 PSMA (Pluvicto) 於治療椅上進行治療，人員進行治療前須戴上手套與鞋套，佩戴輻射佩章但皆無穿鉛衣，其餘大致流程與lutathera 相似．進修過程中亦觀察進行中的臨床試驗：Ac-225 DOTATATE treatment，流程目前與 Lutathera一致。



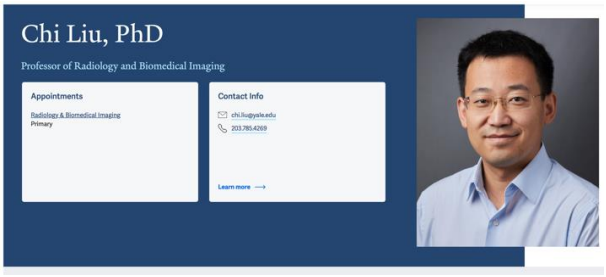
<u>學術研究</u>

正子中心研究會議 Imaging Lab Meeting – 每月安排一次，由正子中心研究員擔任報告主講者，講解研究方法成果與進行討論，以physics 為主，各個projects 輪流報告進度及 receive inputs from other groups. 不定時正子中心專題演講，亦會邀請其他國家的外賓，

Study projects

1. With Prof. Liu



Anatomically and Metabolically Informed Diffusion for Unified Denoising and Segmentation in Low-Count PET Imaging

Menghua Xia[a], Kuan-Yin Ko[b], Der-Shiun Wang[b], Ming-Kai Chen[a], Qiong Liu[c], Huidong Xie[c], Liang Guo[c], Wei Ji[a], Jinsong Ouyang[a], Reimund Bayerlein[d], Benjamin A. Spencer[d], Quanzheng Li[c], Ramsey D. Badawi[d], Georges El Fakhri[a], Chi Liu[a,c,*]

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[b]*Department of Nuclear Medicine, National Taiwan University Cancer Center.*
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ARTICLE INFO

Article history:
Received ** Feb 2025

Keywords:
Positron emission tomography
Multi-task learning
Denoising diffusion model
nnMamba

ABSTRACT

Positron emission tomography (PET) image denoising, along with lesion and organ segmentation, are critical steps in PET-aided diagnosis. However, existing methods typically treat these tasks independently, overlooking inherent synergies between them as correlated steps in the analysis pipeline. In this work, we present the anatomically and metabolically informed diffusion (AMDiff) model, a unified framework for denoising and lesion/organ segmentation in low-count PET imaging. By integrating multi-task functionality and exploiting the mutual benefits of these tasks, AMDiff enables direct quantification of clinical metrics, such as total lesion glycolysis (TLG), from low-count inputs. The AMDiff model incorporates a semantic-informed denoiser based on diffusion strategy and a denoising-informed segmenter utilizing nnMamba architecture. The segmenter constrains denoised outputs via a lesion-organ-specific regularizer, while the denoiser enhances the segmenter by providing enriched image information through a denoising revision module. These components are connected via a warming-up mechanism to optimize multi-task interactions. Experiments on multi-vendor, multi-center, and multi-noise-level datasets demonstrate the superior performance of AMDiff. For test cases below 20% of the clinical count levels from participating sites, AMDiff achieves TLG quantification biases of -26.98±56.76%, outperforming its ablated versions which yield biases of -35.85±67.97% (without the lesion-organ-specific regularizer) and -40.79±62.74% (without the denoising revision module). By leveraging its internal multi-task synergies, AMDiff surpasses standalone PET denoising and segmentation methods. Compared to the benchmark denoising diffusion model, AMDiff reduces the normalized root-mean-square error for lesion/liver by 16.95/5.77% on average. Compared to the benchmark nnMamba segmentation model, AMDiff improves lesion/liver Dice coefficients by 8.94/2.91% on average.

Unified denoising and segmentation in low-count PET imaging

My contribution: identify as well as delineate the contours of tumors for segmentation model comparison

Output:

(1) Co-authors to the abstract submission to 2024 IEEE Nuclear Science Symposium (NSS), Medical Imaging Conference (MIC) and Room Temperature Semiconductor Detector (RTSD) Conference.

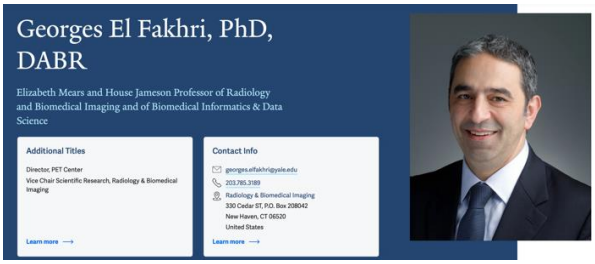
(2) As a co-author to the manuscript, under submission to “Medical Imaging Analysis”

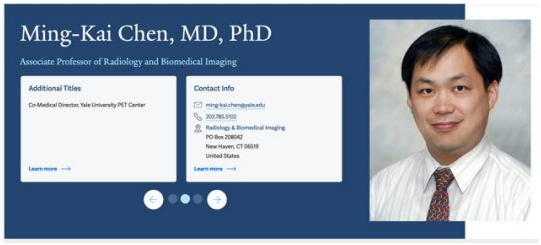
2. With Prof. George

Algorithm in RT planning with PET, focus on head and neck cancer

3.With Prof. Chen

CAR-T treatment related neurotoxicity: PET finding





weekly small groups online discussion

<u>生活面向</u>

OISS 專門為初到耶魯的國際學生、學者及其家屬提供全方位的協助，涵蓋生活各層面，包括食宿、交通、娛樂等。此外，OISS 定期舉辦多樣活動，如英語會話團體、感恩節和聖誕節等節慶活動。正值美國大選期間，特別活動中曾邀請耶魯政治系教授，向國際學生分享美國政治歷史和現狀，例如建國者在制定憲法時如何設計立法制度以防止行政權力過大、美國兩黨對於非法移民的政策、美國社會的政治環境變遷，以及美國醫療保險制度的影響等。這些分享讓國際學生對美國的選舉制度、總統大選及新政府上任對社會和醫學研究的影響有了更深入的了解。

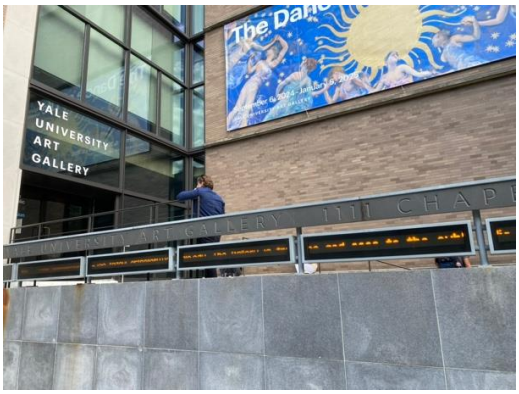
校園安全措施

由於美國許多市中心區域治安不佳，耶魯校方在 New Haven 市內設置了超過 500 部「藍色求助電話」（Blue Phone），這些電話配備攝影監控及緊急求助按鈕。校園保全人員定時巡邏，並推出「Life Security」手機應用程式，讓師生在緊急情況下能即時定位並報警。此

外，學校還提供遍及 New Haven 及周邊地區的免費校車服務（Yale Shuttle）部分路線在夜間提供送至住家門口的安全接送服務。

豐富的文化與藝術資源

耶魯大學擁有豐富的文化和藝術資源。校內的皮博迪自然史博物館（Peabody Museum）與藝術博物館（Art Museum）對外免費開放，館藏豐富，包括恐龍化石及雷諾瓦、梵谷等大師真跡，讓學生和訪客能輕鬆接觸藝術與科學。耶魯的音樂學院與戲劇學院享譽國際，經常舉辦各類音樂會與戲劇表演，票價親民，是難得的文化饗宴與學習機會。



心得及建議

此次進修除了增強醫學知識外，也讓我開闊了視野並豐富了人生經驗。衷心感謝院方及各位師長的支持，並感謝本科同仁在我進修期間協助處理各項業務與臨床工作。從準備階段到踏入耶魯校園和醫院，每一步都讓我感受到耶魯完善的制度與周全的安排，包含交通車的安排，建議院區的交通車或許也能採用動態即時地圖，使乘客容易辨識車輛行經的路線與所在位置。最後，無論是進修計畫的規劃、與耶魯 OISS 和 YNHH 工作人員的信件聯繫，還是行前的食衣住行安排及在美期間參與的各項活動，整個過程能有條理地順利完成，這對我而言是一項寶貴的挑戰和成長機會。這次的進修在學術、臨床實務以及個人成長方面，都讓我受益匪淺，期盼未來能與耶魯大學建立更深厚的聯繫，開展更多合作機會。