臨床正子放射斷層攝影

關少雄 顏國揚 周明仁 編著

合記圖書出版社 發行

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前　言

正子放射斷層攝影（Positron Emission Tomography, PET）雖然已應用了十數年，在台灣開始裝置掃描儀（Scanner）及迴旋加速器（Cyclotron）亦快有十年的時間，但是一直以臨床研究為主，自1999年私立中山醫學院在附設醫院裝置迴旋加速器及三台掃描儀後，即主以臨床檢查為主，研究部份則以病例收集分析為主，這樣的做法使檢查範圍更為廣泛，數目更為快速增加，自此相繼在台北長庚醫院、新光醫院陸續購置掃描儀，台北榮總亦更新機型加入推廣PET作為臨床應用之行列，在不久的將來，中南部亦會有增設新PET中心的趨勢，更高的檢查頻率即將來臨。

在眾多醫療人員參與PET工作行列時，自然會很希望能有一些基本參考資料，尤其在讀片時更想有一些參考的圖像，在國外已出版的PET專門書本不多，而且許多圖像還是用較早機型做出的，在台灣或亞洲地區則仍未見到一本所謂「本土」化的PET圖譜，筆者收集較清澈且較確定診斷的圖像，約二百多張，其中包括惡性腫瘤圖像、非癌症但有臨床參考價值圖像、腦部圖像及心臟圖像等，並配合一些可讀性高的有關文章結集成書，使臨床醫師及有關學系的學生作為參考材料或補充讀物。

此書的出版自屬「野人獻曝」但亦有「拋磚引玉」之意，因編集書寫時間很短，付梓又匆促，錯誤漏失之處自所難免，請識者與讀者包涵及指正。

Preface

Although Positron Emission Tomography (PET) have been applied as a part of the medical field in Taiwan for almost ten years. However, it was initiated exclusively for research purpose until Chung Shan Medical and Dental College installed in its affiliated hospital a PET Center facilitated with three PET scanners and a cyclotron in August 1999. Clinical studies became the primary goal of the PET center. Research conducted would strictly involve case data collection and analysis. In turn, the scope of service broadened and the numbers of study accumulated faster.

Acknowledge as the pioneer in Positron Emission Tomography clinical service in Taiwan, The Chung Shan PET Center served as examples for other hospitals in Taiwan. The Chang Kang Memorial Hospital and Shin Kuang Hospital followed to install new PET scanner in their hospital in August 2000 and February 2001 respectively. During July of that year The Taipei Veteran General Hospital upgraded their facility by installing a new model of PET scanner, enabling the hospital to initiate clinical studies as opposed to the research based agenda. Imminent are hospitals in the Southern and Central Taiwan to develop more PET Centers to join in the field of clinical PET. The frequency of examination and the sum of study are certain to increase tremendously.

With the ever increasing number of medical professionals in the PET field, references especially imaging are inevitably needed. Up to this date only a few published PET textbooks are available, with some using images produced by older model scanners. And most certainly a PET book in Chinese does not exist. This book is a collection of articles pertaining to PET studies and diseases. Included are over 200 PET pictures of cancer images, non-malignancy variant images, brain images, and cardiac images. The articles are exclusively written in Chinese and the explanation or data of PET images are in both Chinese and English. This book can be used as a reference for clinicians and serve as supplements to textbooks for students of related fields.

The collection of various images and composed writings were prepared in a relatively short time span before they were sent for print. Thus mistakes or omissions are inevitable. Your comments and suggestions are appreciated for the next edition.

The author

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第1章

正子放射斷層攝影介紹

Introduction to Clinical PET

1.1 正子放射斷層攝影

Positron Emission Tomography

除了基本的X光照片外，電腦軟體的廣泛應用，電腦斷層掃描（CT）、磁共振造影（MRI）、超音波掃描（Ultrasound）、各種血管攝影（Angiography），以至核子醫學單光子射出斷層掃描（SPECT）及正子放射斷層攝影（PET）跟著迅速發展，提供臨床上的應用。影像醫學是近代診斷醫學中進步相當快的一項科學。正子放射斷層攝影術（Positron Emission Tomography，PET）尤其是一門發展快速的嶄新影像技術。其方法是將經由放射核種標化的核子藥劑，以靜脈注射或吸入的途徑注入人體後，再使用正子放射斷層攝影儀予以追蹤測定，藉以瞭解該放射性追蹤劑在體內分佈的狀況。正子放射斷層攝影術所使用的核子藥劑多屬生命基本物質或其衍生物之標化物，所以可以提供活體中生理和生化活動的訊息。由於絕大多數人類疾病發生的初期，其生化方面的變化常在解剖變化出現之前，正子放射斷層攝影術，則能精確地提供這方面質與量的資訊，而且在檢查過程中對受檢者又不會造成傷害，因此可以得到正確的『早期診斷』，進而能『早期治療』，無論對生命的延長或生活品質的維持，PET佔有重要的地位。

PET的造影原理

正子放射斷層攝影術（PET）與傳統造影術之基礎差異性在於：PET所使用的核子藥劑，是經過標化具有高度專一性的生命機質或其衍生物或某些特定藥物，可以針對某特定組織或器官，以定量方式測定其單位體積內的放射性濃度，藉此以瞭解該組織或器官對該物質的代謝情形，進而探討疾病的致病轉機，因此，PET所提供的是有關活體的生理、生化和代謝活動方面的資訊。X光電腦斷層攝影術（X-ray Computerized Tomography, CT）和磁共振造影（Magnetic Resonance Imaging, MRI）的影像所提供的資訊，只屬解剖和結構方面的變化，單光子放射斷層攝影術（Single-Photon Emission Computerized Tomography, SPECT）雖屬三度空間造影，然而因爲所使用的是傳統的核子藥劑，故僅能獲得功能影像，唯獨只有PET才能提供有關生理、生化和代謝方面的量化資訊。

迴旋加速器（Cyclotron）

PET檢查所用的追蹤劑是由迴旋加速器生產製造的，迴旋加速器利

用離子經過電磁場運轉加速，形成一高能量的離子束，導引至靶體上，撞擊靶內物質產生帶正子的新核種，再將核種配入人體內所用的物質如：葡萄糖、氨基酸、水等，製造成可用的追蹤劑（Tracer）。

追蹤劑（Tracer）

將追蹤劑注入或吸入人體內，由於核種的衰變而放出正子（Positron），正子與電子物理特性相同，只是本身帶的是正電，當正子行走很短的距離時，即遇上細胞中帶負電之電子（Electron），產生互毀反應（Annihilation Reaction）形成一對方向相反各帶511KeV的加瑪射線，自體內向外發出。PET所使用之追蹤劑多爲碳-11（^{11}C）、氮-13（^{13}N）、氧-15（^{15}O）及氟-18（^{18}F），它們的半衰期最短爲^{15}O的二分鐘，最長爲^{18}F的110分鐘。應用上一般而言，^{11}C用於心肌氧化偵測，^{15}O用於腦血流測量，^{13}N用於心肌血流測量，^{18}F半衰期最長則可用於腫瘤、心臟及中樞神經的檢查，是目前採用最廣泛的追蹤劑。

斷層掃描（Tomography）

掃描儀（Scanner）是利用結構上環形分佈的眾多偵測器（Siemens ECAT EXACT HR$^+$內有18,432個Detector）去收集由正子與電子互毀後產生的加瑪射線，經電腦運算重組及綜合血液中正子放射物濃度的變化，獲得功能圖像及各種功能參數，如細胞的糖代謝率等。圖像形成後即可供臨床對人體內細胞代謝情形的瞭解，進而診斷出其正常與病變的程度。

結論

PET的特性為：

(1) 所使用之同位素係身體所有之生化元素，可直接參與生理代謝反應。

(2) 同位素之半衰期短，可多次加以使用。

(3) 屬非侵襲性且具高靈敏度準確度。

(4) 同位素活性之分佈，可精確的定位，提供定量性資料等。

因此若是要對疾病做有效的預防和治療，臨床上便須要一種具有高靈敏度和專一性，又能提供有關代謝訊息的診斷方法，而正子放射斷層攝影術（PET）正好符合這些條件，進而成爲對人體生理、生化變化研究及臨床診斷的一大利器，更是治療與手術成效評估之最佳工具。

1.2 Positron Emission Tomography

ABEL S. KWAN, M.D., Ph.D.

Introduction

Clinicians have been traditionally trained to interpret information provided by anatomically based imaging techniques. With the advent of molecular biology-based medicine, a transition is being made to incorporate diagnostic interpretation information used on biochemical changes that exist in disease, frequently in the absence of changes in anatomy. Positron emission tomography (PET) measures biochemistry and physiologic function in the human body. Therefore, PET is fundamentally different from computed tomography (CT) and magnetic resonance imaging (MRI), which transmit structural information based on tissue density, proton density or proton relaxation dynamics. CT and MRI are useful for clinical diagnosis when the disease process causes significant structural transformations. In most diseases, chemical changes precede structural alterations that can be detected by PET. Evidences obtained from numerous significant studies show that in a number of diseases, metabolic changes are measurable by PET long before CT or MRI show any evidence of disease. PET is currently the only clinical imaging methodology that can be used quantitatively to assess the biochemical disturbances in tissue in vivo during disease occurred. Therefore, PET has become a very useful adjunct to anatomic imaging techniques, adding unique information to the characterization of disease.

The major applications of PET are in oncology, cardiology and neurology. In oncology, PET is the only technology that can distinguish benign from malignant lesions in most cases, choosing optimal site for biopsy, monitoring response of tumors to therapy, and diagnose recurrent tumor from post surgical changes or radiation necrosis. In cardiology, PET is a non-invasive technique that provides highly accurate determinations of coronary artery disease, with a sensitivity and specificity greater than 95%, which would largely eliminate most of the normal coronary angiograms. PET, in addition, is the sole technology that can accurately determine myocardial viability. The ability of PET in determination of myocardial viability would lead to accurate

selection of patients for revascularization procedures, particularly to those patients who have severely compromised ventricular function. This can lead to significant decrease in mortality and morbidity rates as well as cost savings. In neurology, other than tumor detection, PET has proven value in diagnosing Alzheimer's disease, Huntington's disease, Parkinson disease or multiple-infarct dementia. PET can also determine the focus of seizure for surgical resection.

Production of Positron-emitting Isotopes

Cyclotron

The most useful positron emitters come from stable parent isotopes that cannot be produced in a generator, only a cyclotron. In the cyclotron, stable nuclei are bombarded with protons or deuterons to create the proton-rich state necessary for positron emission. Because of their relatively short half-lives, it is necessary that the cyclotron be built close to the PET scanner. PET centers do not need to own a cyclotron and can receive labeled compounds from regional distribution centers. However, the distribution center should be located within a reasonable distant since the radioisotopes have a relatively short half-life. The technology for medical cyclotrons has advanced dramatically in the last decade. Compact, automated, self-shielding, reliable medical devices with less cost, which can be operated by a single technician, are in the market.

The radioisotopes delivery system (RDS) made by CTI/Siemens is an example of a modern PET cyclotron. It accelerates negative hydrogen ions to 11 MeV. Once the beam of hydrogen ions has reached the desired energy, it is extracted from the cyclotron by passing it through a thin carbon foil which strips off the two electrons. The resulting proton leaves the cyclotron and strikes the target. The advantages of this type of negative ion cyclotron designs include easy control, simplified beam shaping, very little beam loss, and uniform beam intensity distribution. The RDS device can deliver a 50 uA proton beam yielding 2-3 Ci of ^{11}C, ^{15}O or ^{18}F, and 0.6 Ci of ^{13}N. The whole system was so easy to operate that can be managed by one technician sitting at a workstation.

Tracer Synthesis

There are several important considerations in tracer design for PET. First, the half-life of common use tracers are relatively short (^{15}O, 2 minutes; ^{13}N, 10 minutes; ^{11}C, 20 minutes and ^{18}F, 110 minutes), the synthesis of the labeled product must be rapid. Second, whether to produce a natural substrate or an analog is another issue. A natural substrate is the direct substitution of a positron-emitting atom for a stable atom, and an analog is the modification of natural substrate at one or several key location. The analogs can be targeted and limited to interactions in a small section of complex biochemical reaction sequences that can facilitate subsequent analysis and interpretation of the PET data. Finally, the position at which the positron-emitting label is placed is critical. Detailed knowledge of the biochemical reaction sequence is required for chosen of best labeling position. To perform this task, a chemist seems to serve better suited than a pharmacist.

Taking the positron-emitting isotopes from the cyclotron target and synthesizing the labeled tracer of interest can be a labor intensive work. Automated devices for taking the positron-emitting precursor and turning it into labeled compound ready for injection now are available for producing some of the more commonly used PET tracer such as ^{18}F-fluorodeoxyglucose, FDG. These biosynthesizers are integrated directly into the cyclotron, allowing sterile, pyogen-free labeled compounds to be produced automatically without intervention.

PET Scanner

As the labeled tracer, FDG for example, enters into the cells of the body after injection given, the average range of a positron in soft tissue is only a few millimeters. At the end of its range, a positron encounters an electron and undergoes an annihilation reaction in which the mass of the electron and the positron is converted into two 511 KeV gamma rays, which are emitted at 180 degree to each other. If both r rays are detected within a certain time of one another, then it is assumed that they both originated from the same annihilation event, and that the original disintegration occurred along a line joining the two detectors. This is known as annihilation coincidence detection. A PET scanner consists of rings of scintillation detectors, arranged so that pairs of detectors on

opposite sides of the ring operate in coincidence with one another. The scintillator converts the energy of gamma rays into a flash of light, which is detected by the photomultiplier tube and converted to a small current pulse. If two gamma rays were detected simultaneously from opposite sides of the body, then an event is registered and stored. Data can be acquired and reconstructed by a computer into tomographic images of the body using standard algorithms. Commercial PET scanner consists of several rings of BGO block detectors. Many contiguous planes are imaged simultaneously, so that the whole brain or heart can be imaged without moving the patient. For example, Siemens made PET scanner ECAT EXACT HR+ constructed by 18,432 detectors and 63 planes can be imaged simultaneously.

Clinical Use

Cardiac Application

PET imaging of the heart provides an elegant tool for assessing regional coronary blood flow and metabolic processes in myocardial cells. A short half-life tracer ^{13}N ammonia is most commonly use to study myocardial perfusion because it is rapidly cleared from the blood and avidly retained in myocardial tissue. In a large number of studies, clinical applications of PET perfusion imaging in CAD have been established:

1. Accurate, non-invasive diagnosis of CAD in symptomatic or asymptomatic patients;
2. Assessment of physiologic stenosis severity for determination of revascularization;
3. Assessment of response to antiischemic and thrombolytic treatment;
4. Follow-up of progression or regression of CAD;
5. Evaluation of collateral function.

For the evaluation of CAD coronary angiography remains the "gold standard", which provides exact information on the location and anatomic severity of epicardial coronary artery stenosis. However, the physiologic significance of any lesion may be difficult to access from angiographic images alone, and perfusion abnormalities may occur in the absence of arteriographically assessable stenosis. PET represents the most advanced technique, permitting accurate qualitative and quantitative assessment of regional myocardial tracer distribution.

Assessment of tissue viability has become an important application of PET in cardiology. Clinical observations have led to the concept that myocardium may adapt to chronic ischemia by decreasing its contractility, matching the reduced perfusion with reduced energy demand and thereby preserving viability. This phenomenon has been described as "hibernating myocardium". If the ischemia is relieved, the myocardium regains normal contractility. A treatment with revascularization is a crucial decision to these patients. Using ^{18}F-fluorodeoxyglucose (a FDG in the PET process) that measures myocardial glucose utilization, it is possible to identify myocardial tissue that is hypoperfused at rest with preserved or increased glucose uptake. An increased uptake of FDG in relations to myocardial perfusion, or perfusion-viability mismatch, is indicative of hibernating myocardium, whereas matched defects are indicative of scar. The positive and negative predictive values have been reported to range from 80-85%.

Oncology Application

In oncology, PET is the only modality that can accurately image many organs of the body with a single pass to allow determination of malignancy. It provides information to determine whether a primary cancer has metastasized to other parts of the body. PET has demonstrated its usefulness in: cost-effectiveness; whole-body metastatic surveys; avoiding biopsy for low grade tumors; non-invasive differentiation of tumors from radiation necrosis; early change in course of ineffective chemotherapy; and avoiding unnecessary diagnostic and therapeutic surgery.

There are many alterations in cancer physiology that can be detected by PET using positron-emitting tracers. Tumor cells commonly grow more rapidly than normal tissues and thus have higher rates of glucose metabolism, DNA synthesis, and amino acid transport than normal tissues. The major and most common tracer used to trace glucose metabolism is FDG, which is transported into cancer cells and phosphorylated like glucose, but is not substantially moved beyond this point in the intracellular glucose metabolic pathway. In a wild variety of cancers, a high tumor/background uptake ratio develops 30 to 120 minutes after intravenous injection of FDG.