

Multimodality Imaging –PET/CT and PET/MRI: Making a Difference

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Abstract: Last decade has witnessed the significant role of hybrid imaging modalities (PET/CT and PET/MRI) in clinical examinations for diagnostic, therapeutic and other health related conditions of humankind. These modalities provide both the information, i.e., functional and anatomical in the single image relating to the organ under study. Thus, diagnostic accuracy and specificity of the disease in many patient studies has enormously increased. Also, confidence level in therapeutic procedures has risen. In this paper, evolution and clinical use of PET/CT and PET/MRI are briefly reviewed.

Keywords: PET/CT, PET/MRI, Multimodality Imaging Systems, Diagnostic Accuracy, Oncology.

I. INTRODUCTION

Diagnostic imaging is progressively playing a significant role for investigations into human health and diseases. The information extracted from clinical images is used for staging, restaging human diseases and for guidance to the surgical and therapeutic procedures. At present, various diagnostic imaging modalities are in use in clinical practice. For example, some common diagnostic imaging techniques are; X-ray computerized tomography (CT), ultrasound (US), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT), and positron emission tomography (PET). These modalities have been categorized on the basis of their characteristics in providing the morphological (anatomical) and functional information of human body. Some techniques work well to achieve morphologic information but are unable to provide functional information of the organ of interest. On the other hand, better information relating to physiological processes can be obtained by another type of diagnostic imaging modality instead of structural information. However, in clinical practice it is more beneficial to obtain both the anatomical and functional information for proper diagnosis and accurate treatment of disease.

II. EVOLUTION OF PET/CT AND PET/MRI

2.1 PET/CT:

In early 1984 a team of researchers of the University of Gunma, suggested the blending of a full-ring PET and CT. The design was centered upon PET and CT tomography systems positioned side by side with the patient handling system passing through the systems. However, their work was not largely publicised, and the concept was not commercially developed [1].

Later, in early 1990s, Townsend, Nutt and colleagues proposed to integrate PET with X-ray CT and also suggested for PET attenuation correction by generating the attenuation factors using the X-ray CT data as reported in [2]. In 1998, the first PET/CT prototype was designed and developed by CTI PET systems, now known as Siemens Healthcare. The scanner was assessed clinically at the University of Pittsburgh, which was comprised on a single slice spiral CT scanner and a revolving PET scanner (ECAT ART). The PET detectors were attached on the back of the CT support and the whole assembly revolved as one unit. With this prototype PET/CT scanner more than 300 cancer patients went under

clinical examinations [3], [4], [5]. The findings of the prototype proved the significance of high resolution anatomy precisely registered with practical data. Hence, the functional abnormalities were localized and inexplicit situations were clarified and enhanced accuracy as well as confidence of scan analysis was achieved.

The earliest commercial PET/CT imaging system was introduced early in 2001 by GE Healthcare was the Discovery LS. Few months' later Siemens Medical Solution and Philips Medical Systems announced the multimodality imaging systems. In the past few years, due to the development in CT and PET instrumentation, new designs of PET/CT scanners have evolved worldwide. All of the scanners support multi-bed, whole body imaging within one session. For more accurate quantitative metabolic imaging, CT data was applied to compensate PET images for scatter and attenuation [6].

2.2 PET/MRI:

Hybrid imaging scanners, such as, SPECT/CT and PET/CT provide improved diagnostic value in tumor diagnosis and staging [7], [8], [9], [10]. The dual-modality imaging systems are becoming important tools in clinical imaging for diagnosis of disease and exact determination of anatomical location of a tumor, which play a vital role for treatment planning in radiotherapy and surgery. The advantages of combined modalities X-ray CT with SPECT or PET led to the development of the integration of other scanning modalities, e.g., MRI and PET. Though, X-ray CT data provides useful anatomical information, nevertheless it provides inadequate soft-tissue contrast relative to MRI. Furthermore, MRI has higher specificity and sensitivity than CT in oncology [11]. Due to these additional reasons, MRI with PET seems to be a perfect combination of two standalone well established imaging modalities. In terms of radiation dose, X-ray CT exposes patients to higher doses [12].

The idea to combine PET and MRI to make a dual-modality system for clinical examinations arose after the small animal designs in late 1990s [13]. Traditionally and technically, PET/MRI arrangement is more complicated and challenging as compared to the integration of PET (or SPECT) and X-ray CT, e.g., sensitivity of phototubes to even low magnetic fields. Further, because of the interference of magnetic field of MRI scanner to PET equipment which resulted major artifacts in PET images was a hard task to overcome for long time. The new generation of PET/MRI scanners has been developed using semiconductor PET detectors [14], [15].

III. CLINICAL USES OF PET/CT AND PET/MRI

3.1 PET/CT:

In oncology, PET/CT has swiftly come out as an essential instrument [16]. There are several factors that have made PET/CT as a successful medical imaging technique. For the comprehensive diagnostic anatomical and functional information, patient has the advantage to undergo for the examination in one session. It provides more accurate information as compared to PET or CT as standalone modality. In addition, PET/CT allows the radiation oncologist to apply the information obtained from PET for an appropriate plan of radiation treatment.

Results of clinical examinations suggest that, PET/CT provides more accurate results in diagnosis of a large of number diseases relative to PET or CT alone [16]. In oncology, PET/CT differentiates very significantly the malignant from benign disease. It identifies more accurately, the locations of disease and detects the primary tumor which was previously unknown. Also, precisely stages the disease, estimates the prognosis, identifies the residual disease and confirms the sites of recurrence. Furthermore, it has a significant impact on foreseeing the early response after the initiation of the treatment, and objectifying the effectiveness of treatment [17]. Thus, it reflects that PET/CT data are very useful in treatment planning in radiotherapy.

Hybrid PET/CT has a great potential to provide the increased diagnostic information rates as compared to PET or CT alone as well as other techniques when negative results are obtained for patients who have neurologic symptoms indicative of cancer. PET/CT has advantage in brain and cardiac studies over the SPECT/CT [18], [19], [20].

Incorporation of 128-slice CT with PET has met the cardiology demand of faster acquisition, thus PET/CT has turn out to be an ideal cardiac imaging speciality. For instance, enhancing the portrayal of atherosclerotic plaques by scanning the inflammatory procedure related with the plaque – from anatomical and functional information. However, cardiac applications are underdeveloped and recently they have come across some complications, such as, the cardiac and respiratory motion effects. Discrepancy linked with CT based attenuation compensation is more serious for cardiac studies as compared to oncology.

3.2 PET/MRI:

In 2006, Schmand M and his co-workers acquired the first concurrent MR and PET images of the human brain [21]. In recent years, several prototype PET/MRI scanners have been designed for clinical tests. In 2008, a prototype dual-modality PET/MRI system was installed at the University Hospital Tubingen, Germany. A group of researchers led by Thomas Beyer evaluated the system, aiming to demonstrate the feasibility of simultaneous PET/MRI data acquisition of human brain by using avalanche photodiode (APD) based PET detector technology which was integrated into a clinical 3T MAGNETOM Tim Trio system [22]. Their studies indicated that, simultaneous PET/MRI of intracranial tumors using ^{18}F -FDG, ^{11}C -methionine or ^{68}Ga -DOTATOC can be performed reliably.

In 2010, Philips Healthcare has developed a first commercial PET/MRI system. That was installed at the Department of Radiography, Mount Sinai Hospital in New York. Research projects and routine clinical examinations were conducted in order to test and demonstrate the potential of PET/MRI dual-modality imaging in various areas, such as, neurology, cardiology and infectious and inflammatory diseases. Initially, PET/MRI examinations in cardiovascular imaging were conducted to test its utility. Improved image quality of PET/MRI allowed a better visualization and quantification of vascular beds (mainly aorta and carotids). These two devices have been put separately in one room at a 3 meter distance with common sliding patient bed. In fact, scanning with PET/MRI is very complex and requires high degree of expertise. However, it will result in enormous benefits for visualization of tumors.

The use of the hybrid PET/MRI in clinical examinations is in its early stages. However, from preclinical animal studies and numerous patient studies on the use of retrospectively aligned PET or SPECT with MRI shows the significant advantage over the single PET, SPECT and MRI clinical examinations [13], [23], [24]. On the basis of preclinical and clinical studies results, it is reasonable to state that PET/MRI dual modality imaging has to play a leading role in future relative to single imaging modality in certain parts of non-invasive scanning, such as; neurology, oncology and cardiology [23], [25].

In neurology, the use of integrated PET/MRI may potentially provide more than just high contrast image fusion. For example, in brain studies, additional morphological information achieved by MRI may increase the diagnosis accuracy, thus patients' can be managed more properly and accurately. Furthermore, in gliomas examination combined PET/MRI more likely may provide the enhanced diagnostic sensitivity and make it possible to correlate the radiopharmaceutical concentration and the metabolic change in the neoplastic tissue [26].

Several aspects of clinical studies with hardware fused modality PET/MRI still awaits for further investigations and tests. However, this dual modality seems to have a vast potential in the field of neuroscience research, especially, in neural networks for complex function analysis [27].

Applications of PET/MRI modality may potentially increase in oncology, chiefly, it could be more advantageous for detection of tumor in early phases and monitoring of functional therapy. In addition, investigations into the effects of novel drugs may be carried out more precisely and accurately, for example, inhibitors of angiogenesis or immune system modulators. Furthermore, combined information obtained with the dual modality may be more helpful to clarify the mechanism of action and optimize schedule of treatment by studying the metabolism of a cell and microenvironment and their response to treatment.

PET/MRI dual modality may give clinicians the ability to measure the metabolic feasibility of the heart muscle, functional impairment and its perfusion. Furthermore, utilizing the strength of individual modality by integrating them, diverse molecular parameters can be assessed alongside.

In addition, remarkable benefit of accurately simultaneous PET/MRI is that the subject is imaged at the same time with matching environmental factors and stimuli. It is much probable that, such functional studies will advance the boundaries for rudimentary biologic research and will open the doors of new area for studying biology in vivo.

Large number of clinical studies (head and neck) has been conducted in order to compare the performance of PET/MRI and PET/CT, findings of these studies show that in the case of soft tissue imaging PET/MRI has the advantage over the PET/CT [28], [29], [30]. Further, the recent study shows that in oncology both hybrid imaging modalities perform equally well [31].

IV. CONCLUSION

Development of dual modality imaging has paved the way to triple modality imaging and it will be one of the venues of research in future in the area of diagnostic imaging. This may become the ultimate multimodality imaging for multidimensional imaging. The evolution of triple modality imaging will further revolutionize the clinical patient management, clinical research and healthcare in general. However, bringing such modalities to clinical practice will need intensive and careful investigations on prototype design, pre-clinical studies, technological feasibility and cost effectiveness and radiation exposure.

REFERENCES

- [1] Beyer T, Freudenberg LS, Czernin J and Townsend DW, The future of hybrid imaging-part 3: PET/MR, small-animal imaging and beyond. *Insights Imaging* 2011; 2: 235-246, DOI: 10-007/s13244-011-0085-4
- [2] Beyer T, Kinahan P E, Townsend DW and Sashin D 1994 The use of x-ray CT for attenuation correction of PET data *Nuclear Science Symposium and Medical Imaging Conf., 1994 IEEE Conference Record* vol 4 pp 1573, 1577
- [3] Charron M, Beyer T, Bohnen N N, Kinahan P E, Dachille M, Jerin J, Nutt R, Meltzer C C, Villemagne V and Townsend DW 2000 Image analysis in patients with cancer studied with a combined PET and CT scanner *Clin. Nucl. Med.* **25** 905–10
- [4] Klutz P G, Meltzer C C, Villemagne V L, Kinahan P E, Chander S, Martinelli M A and Townsend D W 2000 Combined PET/CT imaging in oncology. Impact on patient management *Clin. Positron Imaging* **3** 223–30
- [5] Meltzer C C, Luketich J D, Friedman D, Charron M, Strollo D, Meehan M, Urso G K, Dachille M A and Townsend D W 2000 Whole-body FDG positron emission tomographic imaging for staging esophageal cancer comparison with computed tomography *Clin. Nucl. Med.* **25** 882–7
- [6] Townsend DW. Multimodality imaging of structures and function. *Phys Med Biol* 2008; 53: 1–39.
- [7] Bar-Shalom R et al (2003) Clinical performance of PET/CT in evaluation of cancer: additional value for diagnostic imaging and patient management. *J Nucl Med* 44(8):1200–1209
- [8] Antoch G, et al. (2004) Accuracy of whole-body dual-modality fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography and computed tomography (FDG-PET/CT) for tumor staging in solid tumors: comparison with CT and PET. *J Clin Oncol* 22 (21):4357–4368.
- [9] Ell PJ. (2005) PET/CT in oncology: a major technology for cancer care. *Chang Gung Med J* 28(5):274–283.
- [10] Pfannenbergl AC, et al. Value of contrast-enhanced multi-phase CT in combined PET/CT protocols for oncological imaging. *Br. J Radiol.* 2007;80(954):437–445.
- [11] Muller-Horvat C, et al. Prospective comparison of the impact on treatment decisions of whole-body magnetic resonance imaging and computed tomography in patients with metastatic malignant melanoma. *Eur. J Cancer.* 2006;42(3):342–350.
- [12] Brix G, et al. Radiation exposure of patients undergoing whole-body dual-modality 18F-FDG PET/CT examinations. *J Nucl. Med.* 2005;46(4):608–613.
- [13] Shao Y, Cherry S R, Farahani K, Slaters R, Silverman R W, Meadors K, Bowery A, Siegel S, Marsden P K and Garlick P B. Development of a PET detector system compatible with MRI/NMR systems. *IEEE Trans.Nucl. Sci.* 1997;44:1167–71.
- [14] Buchbender C, Hartung-Knemeyer V, Beiderwellen K, et al. Diffusion-weighted imaging as part of hybrid PET/MRI protocols for whole-body cancer staging: does it benefit lesion detection? *Eur. J Radiol.* 2013;82:877–882.
- [15] Punwani S, Taylor SA, Saad ZZ, et al. Diffusion-weighted MRI of lymphoma: prognostic utility and implications for PET/MRI? *Eur. J Nucl. Med. Mol. Imaging.* 2013;40:373–385.

- [16] Czernin J, Allen-Auerbach M, Schelbert H. Improvements in cancer staging with PET/CT: literature-based evidence as of September 2006. *J Nucl. Med.* 2007;48(1):78S–88S.
- [17] Vallabhajosula S. 18F-labeled positron emission tomographic radiopharmaceuticals in oncology: an overview of radiochemistry and mechanism of tumor localization. *Semin. Nucl. Med.* 2007;37: 400–419.
- [18] Whitwell JL, Jack C. Neuroimaging in dementia. *PET Clin.* 2007;2:15–24.
- [19] Antonini A, Leenders KM, Vontobel P, et al. Complementary PET studies of striatal neuronal function in the differential diagnosis between multiple system atrophy and Parkinson's disease. *Brain.* 1997;120:2187–2195.
- [20] Knuuti J, Bengel FM. Positron emission tomography and molecular imaging. *Heart.* 2008;94:360–367.
- [21] Schmand M, et al. Brain PET: first human tomograph for simultaneous (functional) PET and MR imaging *J. Nucl. Med.* 2007;48:45P.
- [22] Beyer T, Schwenger N, Bisdas S, Claussen CD and Pichler BJ. MR/PET – Hybrid Imaging for the Next Decade. *MAGNETOM Flash.* 2010;3:19-29.
- [23] Beyer T and Pichler B. A decade of combined imaging: from a PET attached to a CT to a PET inside an MR. *Eur. J Nucl. Med. Mol. Imaging.* 2009;36(1):S1 – S2.
- [24] Pichler BJ, Judenhofer MS and Wehrl HF. PET/MRI hybrid imaging: devices and initial results. *Eur. Radiol.* 2008;18:1077-1086. DOI 10.1007/s00330-008-0857-5.
- [25] Delbeke D, Heiko S, William H, et al. Hybrid imaging (SPECT/CT and PET/CT): improving therapeutic decisions. *Semin Nucl Med* 2009; 39: 308–340.
- [26] Bisdas S, et al. Switching on the lights for real-time multimodality tumor neuroimaging: the integrated positron-emission tomography/MR imaging system. *AJNR.* 2009;31(4):610 – 614.
- [27] Heiss W. The potential of PET/MR for brain imaging. *Eur. J Nucl. Med. Mol. Imaging.* 2009;36 (1):S105 - S112.
- [28] Kubiessa K, Purz S, Gawlitza M, et al. Initial clinical results of simultaneous 18FFDG PET/MRI in comparison to 18F-FDG PET/CT in patients with head and neck cancer. *Eur. J Nucl. Med. Mol. Imaging.* 2014;41:639–648.
- [29] Queiroz MA, Hullner M, Kuhn F, et al. PET/MRI and PET/CT in follow-up of head and neck cancer patients. *Eur. J Nucl. Med. Mol. Imaging.* 2014;41:1066–1075.
- [30] Schaarschmidt BM, Heusch P, Buchbender C, et al. Locoregional tumour evaluation of squamous cell carcinoma in the head and neck area: a comparison between MRI, PET/CT and integrated PET/MRI. *Eur. J Nucl. Med. Mol. Imaging.* 2016;43:92–102.
- [31] Claudio S, Ken H, Johannes C. 18F-FDG PET/CT and PET/MRI Perform Equally Well in Cancer: Evidence from Studies on More Than 2300 patients. *J Nucl. Med.* 2016;57:1-11.