

Hybrid Imaging – SPECT/CT: Making a Difference

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Abstract: With the technological advancements in the medical imaging field, the past decade has witnessed a dramatic evolution of multimodality imaging systems. Scientists, technologists and researchers have been able to bring systems in clinical practice, in which two or more standalone diagnostic imaging modalities have been combined. Some of those multimodality imaging systems are: PET/CT, SPECT/CT, PET/MRI and PET/SPECT/CT. With this technique a patient is scanned in a single session and the desired structural and functional information of the organ of interest is achieved. Recent clinical imaging studies in the areas of cardiology, endocrinology, infection, musculoskeletal and neurology has shown, that with multimodality diagnostic imaging, a significant increase in diagnostic accuracy is achieved, as compared to single diagnostic imaging modality. In this review, emphasis is given to the technical aspects and clinical applications of the SPECT/CT hybrid imaging modality.

Keywords: Hybrid Imaging, SPECT/CT, PET/CT, SPECT, Diagnostic Accuracy.

I. INTRODUCTION

Imaging technological advancement has always been challenging to practitioners how best to optimize them in patient care. Correlative study has long been in use in clinical practice especially in the interpretation of images in nuclear medicine due to major limitations of morphological localization, poor spatial resolution and tissue attention [1]. Physicians have been well aware of the effectiveness in joining anatomical and physiological imaging five decades ago [2], [3]. The most significant diagnostic imaging technological progression to date is hybrid or fusion imaging, where morphology is merged with physiology resulting in a superior diagnostic tool capable of providing morphological and physiological information in one examination [3]. Earlier, the method of comparison of software co-registration were utilized but were limited by technical problems relating to difference in patient positioning, geometries of imaging equipment and displacement of movable structures between studies [1]. The real break-through in this field came, which caught the attention of medical imaging fraternity worldwide, with the development of computed tomography and hybrid positron emission tomography (PET). The PET/CT innovation has been so successful that major medical imaging manufacturers do not offer stand-alone PET scanners. Spurred by this success, SPECT/CT has presently been implemented in the nuclear medicine fraternity compelled by the advantages posed through their experiences with PET/CT. The unveiling of the positron emission tomography and magnetic resonance imaging (PET/MRI) further added impetus to hybrid imaging and the introduction of prototype PET/MRI devices [1], [3]. Hybrid imaging has few reasons behind its acceptance such as the high level of provision in diagnostic information from an examination, better liaising among clinicians and high specificity [4]. The molecular characterization attained via PET and SPECT has taken these imaging techniques to compliment diagnostic information particularly for cancer evaluation thereby making hybrid imaging the primary diagnostic tool in the new era of cancer imaging [1]. However, in this review, emphasis is given to the clinical applications and the technical aspects of the SPECT/CT hybrid modality.

II. TECHNICAL ASPECTS OF SPECT/CT

Single photon emission computed tomography (SPECT) is based on the determination of the concentration of radionuclide tracer over time and space in the organ of interest. As a result, visualization of dynamic physiological and patho-physiological process that identifies the functional characteristics of disease is achieved. On the contrary, images on SPECT do not achieve precise anatomic landmarks for accurate localization and classification of the results. CT diagnoses and characterizes the disease on the basis of morphologic criteria. This provides the information relating to the variations in the size of organ, and the density of tissue as well as their accurate localization and topographic landmarks. However, morphological data do not in essence show a relationship with the metabolic standing of the disease. Reporting suggest the change from SPECT alone to the combination of SPECT/CT could make diagnosis difference in 30% of the cases. Furthermore, SPECT/CT data has proven to be useful for guiding surgical procedures or in finding the target volume for external beam radiotherapy. Though both techniques, SPECT and CT have individually proved to be of good diagnostic performance it has become very imperative to shift the paradigm of standalone diagnostic imaging modality to hybrid imaging for more accurate diagnosis and treatment of disease. Integrating CT into SPECT has proved to be worthy diagnostic tool in medical imaging in which anatomical details may delineate functional and metabolic information. The SPECT/CT multimodality imaging concept is based on early attempt of localization of radionuclide tracer distribution by achieving morphological information in a single imaging system by using transmission sources in CT [5]. Hybrid imaging is technically more challenging and complex but provides useful information for some procedures along with patient examinations. An often overlooked advantage is that CT data is used for SPECT and PET images for attenuation correction [5] and scatter [6] as well as aiding in the correction of the partial volume effect, especially in tumors [7].

Hasegawa and his colleagues developed the first commercial prototype SPECT/CT imaging system at the University of San Francisco with sponsorship from General Electric Healthcare (GE Healthcare). The equipment was a dual head with a variable geometry coupled in a single gantry to an X-ray source of 140 keV and 2.5mA with a sliding ring detector. The same patient couch for data acquisition of emission and transmission images was used by keeping in view the axial displacement between CT and SPECT imaging field. After the introduction of radionuclide into the patient, CT images were taken during the radionuclide uptake period and then SPECT data were collected. The CT data were utilized to produce attenuation coefficient map for SPECT image data to correct for attenuation of gamma photon effects. A number of clinical studies were performed with this integrated instrument particularly that of quantitative estimation of radiation dosimetry in brain tumor patients [8], [9].

Later Siemens and Philips brought the SPECT/CT integrated imaging equipment, In 2004 Siemens introduced *Symbia* series and Philips followed by introducing *Precidence*. Current SPECT/CT systems include that of *Discovery NM/CT 670* (General Electric), *Symbia T Series* (Siemens), and *BrightView X/CT* (Philips). The CT equipment is able to operate at a low tube current if it is used mainly for attenuation correction [5]. This then enhanced lesion localization, thus improving the overall image quality. Early CT component of combined imaging systems were available with various number of CT slice choices and with variable tube currents. The 64-slice CT cardiac, SPECT/CT provided excellent morphological functional quality by utilizing short scanning time, thereby eradicating patient movement artifacts in the image.

Recently SPECT/CT has emerged as a diagnostic imaging tool with high potential in medical imaging. It facilitates to delineate the morphological details from the functional information in the image. Due to this advantage, the utility of SPECT/CT has largely increased in a number of clinical examinations especially in fields such as endocrinology, oncology, cardiology, musculoskeletal, infection and other areas.

III. CLINICAL APPLICATIONS OF SPECT/CT

3.1 Cardiology

For a patient with coronary artery disease (CAD), its diagnostic and the prognostic evaluation requires, myocardial perfusion scans by injecting Tl-201, Tc99m-Sestamibi, Tc99m tetrofosmin radiotracers. The functional severity of angiographically significant stenosis was defined. Attenuation of gamma photon hampers the specificity and limits the diagnostic accuracy. Furthermore, dual-modality SPECT/CT assists much better to correct the SPECT data for attenuation using the CT data for attenuation coefficient maps as compared to common attenuation correction techniques. Hence, diagnostic accuracy is improved by a proper assessment of the diaphragmatic surface. Nonetheless, in apex and left ventricle anterior wall, false positive spurious perfusion defects may appear due to the respiratory and cardiac motion [10].

3.2 Thyroid Cancer

Iodine-131 planar imaging for thyroid cancer is excellent in diagnosing recurrent or metastatic disease but lacks in accurately locating the disease [11]. SPECT/CT enhances variation between physiological and pathological uptake of the iodine in the whole body scan [12] which have a significant bearing on the treatment approach in patients [13]. Alongside providing information by the Iodine-131 scan, the CT contributes significantly in the detection of lung nodules, lytic bone lesions and lymph node metastases. Therefore, the specificity of the method increases where faults resulted from the physiological elimination of radiopharmaceutical are corrected [14] and confirmed with researchers in Europe reporting incremental value of SPECT/CT by 57% [11]. However to the extent which these outcomes improve patient management is still unclear [5].

3.3 Neuroendocrine Tumours, Neural Crest Tumours

In neuro-endocrine tumor patient studies, SPECT/CT imaging allows the eradication of the physiological ambiguity of radiopharmaceutical (source of false positive) with CT providing better anatomic localization of the SPECT lesions [15], [16]. The addition of 40% of relevant clinical information using SPECT/CT was reported over the usage of SPECT alone [17]. However, the difficulty of false negative SPECT findings can't be delineated due to the inborn low resolution and scarcity of intravenous and oral contrast in the CT component. A high end CT component is suggested to be put into effect in the SPECT/CT device in order to allow high quality contrast enhanced CT image acquisition in addition to SPECT [5]. Neural crest tumours like neuroblastoma, ganglioblastoma and pheochromocytoma, Iodine-123 or Indium-131 MetaIodo Benzyl Guanithidine (MIBG) scintigraphy is utilized for primary tumour localization and monitoring metastatic spread pattern with overall high sensitivity of 92% and specificity of 96% [3] and similar to that of attained by PET/CT with Carbon-11-HED as tracer [18]. A substantial role of SPECT/CT in the healing management of neuroendocrine tumours was also reported in 14% of patients [11].

3.4 Lymphoscintigraphy

The sensitivity of SPECT/CT is increased compared to that of SPECT alone as it lacks in anatomical landmarks [5]. Diagnostic efficacy in pilot studies using SPECT/CT was found to increase compared to that of SPECT in various cancers; melanoma [19], head and neck cancer [20], cervical cancer [21], invasive urinary bladder cancer [22], breast cancer [23] and prostate cancer [24].

3.5 Prostate Cancer

Indium-111-Capromab-pendetide (ProstaScint) is seen as a reliable monoclonal antibody imaging agent for the detecting local or nodal occurrence in planar and SPECT imaging. However, poor spatial contrast and suboptimal quality of the images together with lack of anatomical landmarks has limited it from being used widespread [25], [5]. Though, with the advent of SPECT/CT, ProstaScint imaging has indicated notable incremental diagnostic value for clinical implication for diagnosis and mapping for planning of external radiation therapy [26], [27].

3.6 Bone Scintigraphy

Presently SPECT/CT has added diagnostic information by improving localization and classification of bone lesions. Sensitivity and specificity of SPECT/CT is primarily achieved by detecting benign bone conditions with increased bone turnover [10]. However, no additional benefit had been confirmed over the visual fusion of bone SPECT with planar X-ray, CT or MRI. SPECT/CT has the disadvantage of increased radiation dose. In contrast, low dose SPECT/CT may miss osteolytic lesions [28]. A better solution in solving the problem could be by employing SPECT guided CT that is maintained by the hybrid system [29].

3.7 Infections

Gallium-67 scintigraphy, Indium-111 and Technetium-99m labelled white blood cell scintigraphy are mainly used in the visualization of infection. Physiological uptake and excretion together with poor topographical information may hamper scan information [30]. SPECT/CT has proved to be useful in providing improved diagnostic information, better localization and in evaluating extent of infection [31], [32].

3.8 Skeletal Imaging

The role of SPECT/CT in skeletal evaluation is invaluable. The technology not only has enabled accurate localization but has also improved specificity with CT information [5]. SPECT/CT has proved to be a useful imaging tool in localizing

active arthritis, particularly in areas where the configuration and number of joints is intricate [33]. This multimodality imaging is also ideal for the detection of complications in patients arising from bone injuries such as chronic regional pain syndrome and nonunion with more convincing accuracy [34].

IV. CONCLUSION

The hybrid imaging technique (SPECT/CT) in clinical applications has substantially reduced the number of false-negative results and increased the number of true-positive results. Information extracted from multimodality images may contribute to the development of a specific treatment plan that can lead to the best possible care for each individual patient – personalized treatment. In the future more multimodality imaging techniques may appear with various combinations of standalone diagnostic imaging modalities. This may further revolutionize the diagnostic imaging procedures and will have a tremendous impact on the management of patients and ultimately will synergize the healthcare in particular and research in general.

REFERENCES

- [1] Hicks RJ, Lau EWF, Binns DS. Hybrid imaging is the future of molecular imaging. *Biomedical Imaging and Intervention Journal*. 2007;3(3):1-10.
- [2] Wagner HN. A personal history of nuclear medicine. Springer, London, 2005.
- [3] Nosheen F, Maseeh uz Zaman, Gopinath G, Unaiza Z, Wajeaha S, Areeba Z, Rabia T. Hybrid Imaging in Oncology. *Asia Pacific Journal of Cancer Prevention*. 2015;16:5599 – 5605.
- [4] Townsend DW. Multimodality imaging of structures and function. *Phys Med Biol*. 2008; 53: 1–39.
- [5] Leitha T and Staudenherz A. Hybrid PET/CT and SPECT/CT Imaging, *Computed Tomography - Clinical Applications*, Dr. Luca Saba (Ed.), InTech, (2012). DOI: 10.5772/24004. Available from: <http://www.intechopen.com/books/computed-tomography-clinical-applications/hybrid-pet-ct-and-spect-ct-imaging>
- [6] Beyer T, Townsend D W, Brun T, Kinahan P E, Charron M, Roddy R, Jerin J, Young J, Byars L and Nutt R. A combined PET/CT scanner for clinical oncology. *J. Nucl. Med*. 2000;41:1369–79.
- [7] Soret M, Bacharach S L and Buvat I. Partial-volume effect in PET tumor imaging. *J. Nucl. Med*. 2007;48: 932–45.
- [8] Tang HR, Da Silva AJ, Matthey KK, et al. Neuroblastoma Imaging Using a Combined CT Scanner-Scintillation Camera and 131-I-MIBG. *J Nucl. Med*. 2001;42(2):237-247.
- [9] Townsend DW. Multimodality imaging of structures and function. *Phys Med Biol*. 2008;53:1–39.
- [10] Utsunomiya D, Tomiguchi S, Shiraishi S, et al. Initial experience with X-ray CT based attenuation correction in myocardial perfusion SPECT imaging using a combined SPECT/CT system. *Ann Nucl Med*. 2005;19:485–489.
- [11] Ramanna L. Hybrid Imaging: The Best of Both Worlds. <http://www.itnonline.com/article/hybrid-imaging-best-both-worlds>
- [12] Kohlfurst S, Igerc I, Lobnig M. et al. Posttherapeutic 131-I SPECT-CT offers high diagnostic accuracy when the findings on conventional planar imaging are inconclusive and allows a tailored patient treatment regimen. *Eur. J Nucl. Med. Mol. Imag*. 2009;36(6):886-893.
- [13] Yamamoto Y, Nishiyama Y, Monden T, et al. Clinical usefulness of fusion of 131-I SPECT and CT images in patients with differentiated thyroid carcinoma. *J Nucl. Med*. 2003;44:1905-1910.
- [14] Tharp K, Israel O, Hausmann J, et al. Impact of 131I SPECT-TAC images obtained with an integrated system in the follow-up of patients with thyroid carcinoma. *Eur. J Nucl. Med. Mol. Imag*. 2004;31:1435–1442.
- [15] Ozer S, Dobrozensky G, Kienast O, et al. Value of combined CT/SPECT technology for avoiding false positive planar ¹²³I-MIBG scintigraphy. *Nuclear Medicine*. 2004;43:164–170.
- [16] Schillaci O. Functional–anatomical image fusion in neuroendocrine tumors. *Cancer Biother. Radiopharm*. 2004; 19:129–134.

- [17] Gabriel M, Hausler F, Bale R, et al. Image fusion analysis of ^{99m}Tc-HYNICTyr(3)-octreotide SPECT and diagnostic CT using an immobilisation device with external markers in patients with endocrine tumours. *Eur. J Nucl. Med. Mol. Imag.* 2005;32:1440-1451.
- [18] Franzius C, Hermann K, Weckesser M, et al. Whole-body PET/CT with ¹¹Cmeta-hydroxyephedrine in tumors of the sympathetic nervous system: feasibility study and comparison with ¹²³I-MIBG SPECT/CT. *J Nucl. Med.* 2006;47:1635-1642.
- [19] Even-Sapir E, Lerman H, Lievshitz G, et al. Lymphoscintigraphy for sentinel node mapping using a hybrid SPECT/CT system. *J Nucl. Med.* 2003;44:1413-1420.
- [20] Wagner A, Kermer C, Zettinig G, et al. Validity of sentinel lymph-node (SLN) detection following adjuvant radiochemotherapy (RCT) in head and neck squamous cell carcinoma (HNSCC). *Technol. Cancer Res. Treat.* 2007;6(6):655-660.
- [21] Zhang WJ, Zheng R, Wu LY, et al. Clinical application of sentinel lymph node detection to early stage cervical cancer [in Chinese]. *Chin J Canc/Ai Zheng.* 2006;25:224-228.
- [22] Sherif A, Garske U, de la Torre M, Thorn M. Hybrid SPECT-CT: an additional technique for sentinel node detection of patients with invasive bladder cancer. *Eur. Urol.* 2006;50:83-91.
- [23] Gallowitsch HJ, Kraschl P, Igerc I, et al. Sentinel node SPECT-CT in breast cancer: can we expect any additional and clinically relevant information? *Nucl. Med.* 2007;46:252-256.
- [24] Vermeeren L, Valdes Olmos RA, Meinhardt W, et al. Value of SPECT/CT for detection and anatomic localization of sentinel lymph nodes before laparoscopic sentinel node lymphadenectomy in prostate carcinoma. *J Nuc. Med.* 2009;50(6):865-870.
- [25] Petronis JD, Regan F, and Link K. Indium-111 capromab pendetide (ProstaScint) imaging to detect recurrent and metastatic prostate cancer. *Clin. Nucl. Med.* 1998;23(10):672-677.
- [26] Terence Z, Wong TZ, Turkington TG, et al. ProstaScint (Capromab Pendetide) Imaging Using Hybrid Gamma Camera-CT Technology. *AJR.* 2005;184(2):677-680.
- [27] Sodee DB, Sodee AE, Bakale G. Synergistic value of single-photon emission computed tomography/computed tomography fusion to radioimmunoscintigraphic imaging of prostate cancer. *Semin. Nucl. Med.* 2007; 37: 17-28.
- [28] Horger M, Eschmann SM, Pfannenber C, et al. Added value of SPECT/CT in patients suspected of having bone infection: preliminary results. *Arch. Orthp. Trauma. Surg.* 2007;127(3):211-221.
- [29] Romer W, Nomayr A, Uder M, et al. SPECT-Guided CT for Evaluating Foci of Increased Bone Metabolism Classified as Indeterminate on SPECT in Cancer Patients. *Nuc. Med.* 2006;47(7):1102-1106.
- [30] Filippi L, Uccioli L, Giurato L, Schillaci O. Diabetic Foot Infection: Usefulness of SPECT/CT for ^{99m}Tc-HMPAO-Labeled Leukocyte Imaging. *JNM.* 2009;50(7):1042-1046.
- [31] Filippi L, Schillaci O. Usefulness of hybrid SPECT/CT in ^{99m}Tc-HMPAO-labelled leukocyte scintigraphy for bone and joint infections. *J Nucl Med.* 2006;47:1908-13.
- [32] Bar-Shalom R, Yefremov N, Guralnik L, Keidar Z, Engel A, Nitecki S, et al. SPECT/CT using ⁶⁷Ga and ¹¹¹In-labelled leukocyte scintigraphy for diagnosis of infection. *J Nucl Med.* 2006;47:587-94.
- [33] Pagenstert GI, A. Barg A, Leumann AG, et al. SPECT-CT imaging in degenerative joint disease of the foot and ankle. *J Bone Joint Surg. [Br]* 2009; 91-B: 1191-1196.
- [34] Wall HV, Lee A, Magee M, et al. Radionuclide bone scintigraphy in sports injuries. *Semin. Nucl. Med.* 2010; 40: 16-30.