ARC Journal of Radiology and Medical Imaging
Volume 2, Issue 1, 2017, PP 6-11
www.arcjournals.org

Hybrid Technology: From Cars to Diagnosis

Lucio Mango[1*] & Guido Ventroni[1]

[1]*Nuclear Medicine Department* - *"S. Camillo-Forlanini" General Hospital – Rome, Italy*

Corresponding Author:** ***Lucio Mango, *Department of Nuclear Medicine, "S. Camillo-Forlanini" General Hospital, Rome, Italy,* ***Email:*** *l.mango@scf.gov.it*

1. Introduction

Hybrid: A thing made by combining two different elements. *'This footage is no doubt chilling, but I have to tell you now, it's actually a hybrid of fact and fiction*[1]**.**

From motors to biology to literature this combination of reality and fiction is expanded to limits up to now unthinkable.

Hybrid imaging is defined as the fusion of two or more imaging technologies into a single, new form of imaging. Typically, this new form is synergistic, that is, more powerful than the sum of its parts. Hybrid imaging modalities now in existence include ultrasonography (US)/ magnetic resonance (MR) imaging, MR imaging/angiography, computed tomography (CT)/angiography, single photon emission computed tomography (SPECT)/CT, positron emission tomography (PET)/CT, and PET/MR imaging[2].

In this area nuclear medicine has always found at ease by having always been a complex combination of experience, while always respecting the limits imposed by various compromises of different kinds. So that the concept of combining functional information derived by nuclear medicine with those of anatomical nature that can be derived from radiological technologies has not found practitioners of nuclear medicine unprepared to deal with.

Commonly, while images offered by radiological techniques (CT, MRI, Ultrasounds) are immediately comprehensible, particularly from the anatomical point of view, nuclear medicine techniques, apart from bone scanning, which sufficiently resembles the mind's eye of a perception skeleton to pass as an anatomical representation, have often failed to capture the imagination of the clinician[3], as if the functional image were for some reason less valid, lacking the reference to spatial resolution.

Nuclear medicine actually started as a non-imaging specialty with probes used to measure radioactivity in restricted regions of the body, such as the thyroid gland. The first practical form of nuclear medicine imaging was that performed on rectilinear scanners[4]. Because the resulting images were "life-size", they could be easily overlaid on plain X-rays, which were also acquired without magnification. Therefore, "anatomometabolic" imaging is not a new concept.

The development of the gamma camera by Anger increased the capacity for imaging larger regions of the body, than that of rectilinear scanners. Tomographic imaging with radio nuclides actually predates CT, with early attempts dating from 1963[5]. The first human tomographic images with positron emitting isotopes were presented in 1972[6] thus establishing positron emission tomography (PET) on the map of medical imaging technologies, to be joined by single photon emission tomography (SPECT) a year or so later, following on from the pioneering work of the early 1960s[7].

As diseases originate generally from changes in physiological functioning of apparatus, organs and tissues down to the cellular and sub cellular level, often studying the anatomy of such apparatus and organs, may be not enough to recognize the anatomical modifications that these functional changes have acted. But also that any such modification can take a long time before it become evident, even months or years. Therefore, medical doctors typically employ a combination of imaging techniques during the course of diagnosis and subsequent treatment to monitor their patients[8].

The possibility to align images obtained by different techniques was initially solved with the use of sophisticated image fusion software. This turned out easier enough to rigid structures such as the cranium, but in the rest of the body, accurate alignment is difficult. Alternatives to software-based fusion have subsequently become available through instrumentation that combines two complementary imaging techniques within a single gantry. A combined, or hybrid, tomography such as SPECT/CT or PET/CT can acquire co-registered structural and functional information within a single study. The data are complementary allowing CT to accurately localise functional abnormalities and SPECT or PET to highlight areas of abnormal metabolism[8]. Some of the limitations generally described for scintigraphic techniques may be overcome using these hybrid techniques[9, 10].

The CT component of the hybrid system could be low-dose CT, integrated mainly with a SPECT gamma camera, or single-slice or multislice diagnostic CT. The data obtained by low-dose CT have been reported to be valuable mainly for attenuation correction and as anatomic landmarks of the scintigraphic findings[9]. Data obtained by diagnostic CT also provide detailed morphology of the lesions[11, 12].

2. SPECT/CT

The SPECT component of SPECT/CT systems is the same of conventional nuclear medicine systems; the dual-head gamma cameras are generally used for planar and tomographic imaging of single photon emitting radiotracers.

The CT component uses a low resolution CT detector, in the more dated devices, or a variety of multi-slice CT scanners in more recent SPECT/CT systems.

Separate CT and gamma camera devices using common or adjacent mechanical gantries, and sharing the same scanning table are included in SPECT/CT systems.

SPECT/CT systems using a low-dose single- or multi-slice CT have both the SPECT and the CT detectors mounted on the same rotating platform. Imaging is performed while the detectors are rotating sequentially around the patient. While this concept has the advantage of using the gantry of a conventional gamma camera for both imaging modalities, it limits the rotational speed of the SPECT/CT option to approximately 20 seconds per rotation.

The SPECT component of the SPECT/CT procedure is performed using the acquisition protocols routinely employed for the dual-head gamma camera equipped with collimators adequate for the specific radioisotope in use, CT images are obtained immediately following the SPECT acquisition. Co-registered CT and SPECT are acquired by translating the patient from one detector to the other while the patient remains lying on the same table. This allows the CT and radionuclide images to be acquired with a consistent scanner geometry and body habitus, and with a minimal delay between the two acquisitions.

From the clinical point of view the application of such an imaging system is particularly used for those performances which involve a radiopharmaceutical distribution hard to be attributed to a specific anatomical region. The data obtained from the CT component also make it possible to obtain attenuation-corrected scintigraphic data, thus improving on the quality of the SPECT image alone[13].

For example SPECT/CT studies as an add-on to scintigraphy have been extensively applied to evaluate infectious diseases in various clinical scenarios. Such a technique can usefully be employed in bone infections including the skull and the jaw, as well as the appendicular skeleton, axial skeleton and orthopaedic prosthetic infection. But SPECT/CT can also usefully be employed in soft-tissue infection as cardiovascular or inflammatory bowel disease[14].

Also in **cardiac** field for example SPECT/CT showed that the hybrid approach resulted in a significant improvement in specificity (from 63 to 95%) and positive predictive value (from 31 to 77%) compared with CT alone for detecting flow-limiting coronary stenoses[15]. Sato et al.[16] showed that adding SPECT information in non-evaluable arteries on CTCA improved particularly specificity and positive predictive value of the latter techniques significantly (from 80 to 92%, and from 69 to 85%, respectively). Hence, hybrid cardiac imaging may facilitate the identification of haemodynamically significant coronary artery stenoses and thereby guide clinicians on the appropriate method of revascularization[17]. Hybrid or multi-modality imaging is often applied in the evaluation and management of cardiovascular disease. While recent advances in techniques of fusion imaging software and hybrid imaging systems have enabled efficiency of multimodal imaging, access to the full potential of this technique requires the development of a new set of tools for multimodal contrast agents that improve the process of imaging. Some researchers[18] report the development of a hybrid probe for both SPECT and CT imaging that facilitates high sensitivity SPECT and high spatial resolution

CT imaging, a novel intravascular, multimodal dendrimer-based contrast agent for use in pre-clinical SPECT/CT hybrid imaging systems.

The purpose of **bone** imaging is to identify early bone involvement, to determine the full extent of the skeletal disease, to assess the presence of accompanying complications, such as fractures and cord compression, and essential for optimal therapy of oncologic patients and to monitor response to therapy[19]. The addition of SPECT to the acquisition protocol of body scan has been reported to improve its diagnostic accuracy for detecting malignant bone involvement since is more sensitive in detecting bone lesions than planar scintigraphy and the addition of SPECT/CT systems further improves the allocation to a specific anatomical area in the context of the bone, particularly at the spinal level and in the vicinity of physiologic uptake sites. Thus improving the diagnosis of bone metastases results in a more accurate use of new radiopharmaceuticals with bone tropism for therapy, such as 223radium[20, 21], and reinforcing the concept of "theranostics" in nuclear medicine[22].

Anyhow the SPECT/CT shows a great usefulness in all cases where the distribution of the function is not properly correlated with the anatomical region involved by the disease.

3. PET/CT

The proposal to combine PET with CT was made in the early 1990s by Townsend, Nutt and co-workers[23], and the first intended application of CT images combined with those of PET was that of using them for the attenuation correction[24].

All PET/CT systems permit multi-bed, whole-body imaging within a single examination, using the CT for attenuation and scatter correction of the PET data, as a prerequisite to quantitative metabolic imaging.

PET/CT provides more accurate diagnostic information than PET or CT alone. Further, PET/CT imaging allows radiation oncologists to use the functional information provided by PET for radiation treatment planning[23].

There is, at least for oncology, a growing body of literature that supports the accuracy of staging and restaging with PET/CT compared with either CT or PET acquired separately.

In particular the diagnostic performance of nuclear medicine procedures needed in **lung cancer** patients is testified by the diagnostic impact of integrated PET/CT scanners. These are the differentiation of indeterminate lung lesions, the staging of nonsmall cell lung cancer (NSCLC) for lymphnodes and extrathoracic metastases, the detection of recurrent lung cancer, and the use in small cell lung cancer (SCLC)[25].

Improved accuracy in primary diagnosis, staging and restaging has been documented for a **variety of cancers**, including head and neck, thyroid, lung, breast, oesophageal, colorectal, lymphoma, sarcoma, gastrointestinal stroma tumour (GIST), carcinoma of unknown primary, and melanoma[23].

An application on which PET/CT is also having an impact is that of **radiotherapy** treatment planning[26]. From the beginning, PET/CT provided more convenient and routine access to fused CT and PET images[27]. The most commonly used functional imaging modality for radiotherapy planning is undoubtedly 18F-FDG PET. The convenience of having fused CT and PET images for every patient immediately following the PET/CT could not be matched by even the most sophisticated software. PET/CT systems are contributing directly to the definition of treatment volumes on CT-based plans[28]. Further, the intensity-modulated radiation therapy (IMRT) and the availability of radiotherapy devices to treat tumors with surgical precision by means of sophisticated robotic techniques will continue to increase the demand for PET exams.

Another expanding ground application of the PET/CT in tumors consists in the early response to **therapy monitoring**. In fact the role of PET and PET/CT in the management of patients presenting with cancer is shifting from early staging and later restaging after recurrence to early assessment of treatment response[29, 30]. ^{18}F-FDG PET or PET/CT is able to distinguish early responders from patients resistant to the treatment plan, with significant consequences. This is demonstrated in lymphomas, breast cancer, non–small cell cancers, oesophageal cancer, colorectal cancer and other malig nancies, such as ovarian cancer, uterine cancer, head and neck squamous cell carcinoma, sarcoma, mesothelioma, and melanoma[31].

4. PET/MRI

Early diagnosis and therapy are increasingly operating at the cellular, molecular, or even at the genetic level. Since the diagnostic techniques tend to go from the systems to the molecular level, the role of multimodal molecular imaging such as positrons emission tomography (PET) and magnetic resonance imaging (MRI) that are potent in vivo molecular imaging techniques, is becoming increasingly important[32]. Since 1997 arose the idea of matching these two techniques in a single device, despite technical difficulties that include avoiding the use of any conducting or ferromagnetic materials in the PET detectors, maintaining the homogeneity of the main magnetic field, and minimizing electromagnetic interference (EMI) between PET and MRI signals[33].

Since attenuation correction of positron emission tomographic (PET) data is critical in providing accurate and quantitative PET volumes, deriving an attenuation map (K-map) from magnetic resonance (MR) volumes is a challenge in PET/MR hybrid imaging[34].

The initial euphoria about the medical prospects of PET/MRI is understandable, nevertheless the high cost of integrated PET/MRI systems must be considered to establish what level of hardware integration is really mandatory to meet clinical requirements[35].

It is reasonable to expect that brain PET/MRI will provide disorders, such as neuro degeneration, brain ischemia, neuro-oncology, or seizures[36, 37].

Whole-body PET/MRI will be of particular medical importance because systemic disorders such as cardiovascular disease and cancer increasingly account for morbidity and mortality[35].

Although for years computed tomography (CT) has been the basis for radiation therapy (RT) treatment planning and is still the main imaging modality for precise dose planning and target volume definition, state-of-the-art RT planning is increasingly based on additional imaging modalities. The development of a RT table overlay and RF coil holders and the systematic evaluation provides the technical basis for integration of PET/MR hybrid imaging into RT treatment planning[38].

5. Nuclear Medicine/Optical

Optical measurements [fluorescence-mediated tomography (FMT)] show exquisite congruence to radionuclide measurements and that information can be seamlessly integrated and visualized. This is the case of hybrid PET/OPTICAL or the hybrid sentinel node tracer indocyanine green-99mTc-nanocolloid (radioactive and fluorescent)[39, 40]. This hybrid imaging method has at least three distinct applications: a. It is an experimental tool of displaying different biological processes in vivo in parallel and in real time; b. It may accelerate the development of the chemistry of PET probes; c. It could advance the clinical management of cancer patients[39].

In the case of sentinel node identification, its accurate preoperative mapping using nuclear medicine (lymphoscintigraphy with or without SPECT/CT) and intraoperative radioguidance are vital for planning and performing nodal resection particularly during the sampling of pelvic sentinel nodes originating from prostate cancer. Since the hybrid tracer indocyanine green-99mTc nanocolloid (ICG-99mTc-nanocolloid) was clinically introduced for sentinel node biopsy, the anatomical locations derived from the SPECT/CT images were used to position the fluorescence laparoscope or, when intraoperative fluorescence imaging did not provide accurate identification, to guide resection of sentinel nodes.

References

[1] https://en.oxforddictionaries.com/definition/hybrid

[2] H Hricak, BI Choi , AM. Scott, K Sugimura, A Muellner , GK. von Schulthess, MF Reiser, MM. Graham , N Reed Dunnick, SM. Larson: Global Trends in Hybrid Imaging *Radiology* 257:498, 2010

[3] RJ Hicks, EWF Lau, DS Binns: Hybrid imaging is the future of molecular imaging *Biomed Imaging Interv J* 3(3):e49, 2007

[4] WH Blahd: Ben Cassen and the development of the rectilinear scanner. *Semin Nucl Med* 26(3):165, 1996

[5] HN Wagner: A personal history of nuclear medicine. Springer, London, 2005

[6] R Nutt: The history of positron emission tomography. *Mol Imaging Biol* 4(1):11, 2002

[7] R Jaszczak: The early years of single photon emission computed tomography (SPECT): an anthology of selected reminiscences. *Phys Med Biol* 51:R99, 2006

[8] T Beyer, LS Freudenberg, DW Townsend, J Czernin: The future of hybrid imaging—part 1: hybrid imaging technologies and SPECT/CT. *Insights Imaging* 2:161, 2011

[9] Z Keidar, O Israel, Y Krausz: SPECT/CT in tumor imaging: technical aspects and clinical applications. *Semin Nucl Med* 33:205, 2003

[10] L Kostakoglu, R Hardoff, Mirtcheva, R SJ Goldsmith: PET/CT fusion imaging in

differentiating physiologic from pathologic FDG uptake. *Radiographics* 24:1411, 2004

[11] U Metser, H Lerman, A Blank, G Lievshitz, F Bokstein, E Even-Sapir Malignant involvement of the spine: assessment by 18F-fluorodeoxyglucose PET/CT. *J Nucl Med* 45:279, 2004

[12] Clinical Applications of SPECT/CT: New Hybrid Nuclear Medicine Imaging System. *IAEA-TECDOC-1597*, 2008

[13] O Schillaci: Hybrid SPECT/CT: a new era for SPECT imaging? *Eur J Nucl Med Mol Imaging* 32:521, 2005

[14] PA Erba, O Israel: SPECT/CT in infection and inflammation. *Clin Transl Imaging* 2:519, 2014

[15] S Rispler, Z Keidar, E Ghersin, A Roguin, A Soil, R Dragu, D Litmanovich, A Frenkel, D Aronson, A Engel, R Beyar, O Israel: Integrated single-photon emission computed tomography and computed tomography coronary angiography for the assessment of hemodynamically significant coronary artery lesions. *J Am Coll Cardiol* 49:1059, 2007

[16] A Sato, T Nozato, H Hikita, S Miyazaki, Y Takahashi, T Kuwahara, A Takahashi, M Hiroe, K Aonuma: Incremental value of combining 64-slice computed tomography angiography with stress nuclear myocardial perfusion imaging to improve non-invasive detection of coronary artery disease. *J Nucl Cardiol* 17:19, 2010

[17] O Gaemperli, FM Bengel, and PA Kaufmann: Cardiac hybrid imaging *European Heart Journal* 32:2100, 2011

[18] JM Criscione, LW Dobrucki, ZW Zhuang, X Papademetris, M Simons, AJ Sinusas, TM Fahmy: Development and application of a multimodal contrast agent for SPECT/CT hybrid imaging *Bioconjug Chem* 22(9): 1784, 2011

[19] E Even-Sapir: Imaging of malignant bone involvement by morphologic, scintigraphic, and hybrid modalities *J Nucl Med* 46:1356, 2005

[20] L Mango, M Pacilio: Therapy with Alpha Rays *Arc Journal of Radiology and Medical Imaging* 1(1):1, 2016

[21] M Pacilio, G Ventroni, B Cassano, P Ialongo, L Lorenzon, E Di castro, F Recine, CN Sternberg, L Mango: A case report of image-based dosimetry of bone metastases with Alpharadin (223Ra-dichloride) therapy: inter-fraction variability of absorbed dose and follow-up *Annals of Nuclear Medicine* 30:2, 2015

[22] L Mango: Theranostics: A Unique Concept to Nuclear Medicine *Highpubs J of Cancer Sci Res* 1:001, 2017

[23] T Beyer, DW Townsend, J Czernin, LS Freudenberg: The future of hybrid imaging-part 2: PET/CT *Insights Imaging* 2:225, 2011

[24] P. E. Kinahan,D. W. Townsend, T. Beyer, and D. Sashin: Attenuation correction for a combined 3D PET/CT scanner. *Med Phys* 25(10):2046, 1998

[25] D Hellwig, R Baum, C Kirsch: FDG-PET, PET/CT and conventional nuclear medicine procedures in the evaluation of lung cancer: a systematic review. *Nuklearmedizin* 48(2):59, 2009

[26] E. Ford, J Herman, E Yorke, RL Wahl: 18F-FDG PET/CT for image-guided and intensity-modulated radiotherapy. *J Nucl Med* 50(10):1655, 2009

[27] A-L Grosu, M Piert, WA Weber, B Jeremic, M Picchio, U Schratzenstaller, FB. Zimmermann, M Schwaiger, M Molls: Positron emission tomography for radiation treatment planning. *Strahlenther Onkol* 8:483, 2005

[28] P Dirix, V Vandecaveye, F De Keyzer, S Stroobants, R Hermans, S Nuyts: Dose Painting in Radiotherapy for Head and Neck Squamous Cell Carcinoma: Value of Repeated Functional Imaging with 18F-FDG PET, 18F-Fluoromisonidazole PET, Diffusion-Weighted MRI, and Dynamic Contrast-Enhanced MRI *J Nucl Med* 50:1020, 2009

[29] BE Hillner, BA Siegel, D Liu, AF Shields, IF Gareen, L Hanna, S Hartson Stine, R Edward Coleman: Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the National Oncology PET Registry. *J Clin Oncol.* 26:2155, 2007

[30] ME Juweid, BD Cheson. Positron emission tomography and assessment of cancer therapy. *N Engl J Med* 354:496, 2006

[31] S Ben-Haim, P Ell: F-FDG PET and PET/CT in the Evaluation of Cancer Treatment Response *J Nucl Med* 50:88, 2009

[32] H Zaidi, A Del Guerra: An outlook on future design of hybrid PET/MRI systems. *Medical Physics* 38(10):5667, 2011

[33] Y Shaoyk, SR Cherryy, K Farahaniz, K Meadorsy, S Siegely, RW Silvermany, PK Marsdenx: Simultaneous PET and MR imaging *Phys. Med. Biol*. 42: 1965, 1997

[34] BK. Navalpakkam, H Braun, To Kuwert, HH. Quick: Magnetic Resonance-Based Attenuation Correction for PET/MR Hybrid Imaging Using Continuous Valued Attenuation Maps *Invest Radiol* 48: 323, 2013

[35] BJ Pichler, A Kolb, T Nagele, H-P Schlemmer: PET/MRI: Paving the Way for the Next Generation of Clinical Multimodality Imaging Applications *J Nucl Med* 51:333, 2010

[36] WD Heiss: The potential of PET/MR for brain imaging. *Eur J Nucl Med Mol Imaging* 36(suppl 1):S105, 2009

[37] A Ciarmiello, L Mansi (eds): PET/CT and PET/MRI in neurology. SWOT analysis applied to hybrid imaging Springer International Publishing Switzerland, 2016

[38] DH Paulus, D Thorwath, H Schmidt, HH Quick: Towards integration of PET/MR hybrid imaging into radiation therapy treatment planning *Med. Phys.* 41 (7):072505-1**,** 2014

[39] M Nahrendorf, E Keliher, B Marinelli, P Waterman, P Fumene Feruglio, L Fexon, M Pivovarov, F Swirski, MJ Pittet, C Vinegoni, R Weissleder: Hybrid PET-optical imaging using targeted probes *PNAS* 107(17): 7910, 2010

[40] GH KleinJan, NS van den Berg, J de Jong, EM Wit, H Thygessen, E Vegt, HG van der Poel, FWB van Leeuwen: Multimodal hybrid imaging agents for sentinel node mapping as a means to (re)connect nuclear medicine to advances made in robot-assisted surgery *Eur J Nucl Med Mol Imaging* 43:1278, 2016.

Citation: *Lucio Mango & Guido Ventroni. Hybrid Technology: From Cars to Diagnosis. ARC Journal of Radiology and Medical Imaging. 2017; 2(1):6-11.*