Open Medscience

Peer-Reviewed Open Access

JOURNAL OF DIAGNOSTIC IMAGING IN THERAPY

Journal homepage: www.openmedscience.com

Editorial Review

Inaugural Editorial Review - Nuclear Medicine, Diagnostic Imaging and Therapy

Andrea Ciarmiello[1] and Luigi Mansi[2]

[1]Nuclear Medicine Department, S. Andrea Hospital, La Spezia, Italy
[2]Nuclear Medicine Unit, Department of Clinical and Experimental Internistic 'F.Magrassi, A.Lanzara', Seconda Università di Napoli, Napoli, Italy

Author to whom correspondence should be addressed:
Andrea Ciarmiello, M.D.
Editor-in-Chief
Journal of Diagnostic Imaging in Therapy
editorial@openmedscience.com

Journal of Diagnostic Imaging in Therapy (JDIT) is published online by Open Medscience, based in Northern Ireland, UK. The aim of this new journal is to address the requirements of researchers - specialising in Nuclear and Medical Sciences - by providing open access to peer-reviewed articles. These high quality published articles on Nuclear and Medical sciences are available in both HTML and PDF formats. The published articles are to highlight the application of Diagnostic Imaging with radionuclides, X-rays, magnetic resonance (MR), ultrasound (US) etc. The scope of these imaging modalities include: positron emission tomography (PET), single photon emission computed tomography (SPECT), hybrid imaging systems, radioguided surgery (RGS) and positron emission mammography (PEM). Also included are the application of short and long-lived radioisotopes in research alongside the development of imaging agents and related targeted therapies. In addition,

http://dx.doi.org/10.17229/jdit.2015-0202-011

ISSN: 2057-3782

JDIT's scope will include magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US) imaging and planar X-ray (digital, analogue and portable) systems.

Since the conception of JDIT in the latter part of 2014, we have had the pleasure to receive a variety of research articles, reviews, commentaries, perspectives and case reports ranging from topics on the use of PET imaging, automated radiosynthesis, ^{18}F-FES-PET/CT imaging of breast cancer, prostate cancer therapy and imaging, PET/CT imaging of neuroendocrine tumours using ^{68}Ga-somatostatin analogues, targeted radionuclide therapy, transcranial sonography applications for movement disorders, the application of ^{18}F-fluoride as a marker of unstable atheroma and the use of radionuclides in diagnostic imaging and therapy. These published articles have all been peer-reviewed by the journals' editorial board and/or external reviewers. Here, we would personally like to take this opportunity to thank everyone on the journals' editorial board who has volunteered their time to review these articles.

In this editorial review, we have summarized all the abstracts from the 2014 inaugural issue.

PET Imaging

The first article in the inaugural issue of JDIT was by Grachev *et al.* entitled '*Quantitative in vivo Imaging of Adenosine A_{2A} Receptors in the Human Brain Using ^{11}C-SCH442416 PET: A Pilot Study*.' This research article gave an account of a PET study that showed that the ligand ^{11}C-SCH442416 can be utilized in the A_{2A} receptor binding to quantify the striatal regions of the human brain. Literature precedents have shown that this PET ligand ^{11}C-SCH442416 has been used in preclinical studies by the use of rodents and primates. These studies concluded that ^{11}C-SCH442416 was the first non-xanthine radioligand to demonstrate *in vivo* imaging of adenosine A_{2A} receptors by using PET.

The PET study involved a group of 5 male subjects being injected with 364 MBq of ^{11}C-SCH442416, followed by dynamic PET scanning lasting 90 minutes. During this scanning period emission data was obtained and also arterial blood samples were taken from the patients with the aim of generating an arterial plasma input function.

Magnetic Resonance imaging (MRI) was also used on the patient group to define the various brain regions which included cerebellum, caudate, putamen and thalamus. This process was complemented by applying spectral analysis to determine the frequency components of ^{11}C-SCH442416 and the tissue response in generating regional and voxel time-activity curves (TACs).

The authors demonstrated that ^{11}C-SCH442416 was rapidly metabolized in blood. The unmetabolized PET tracer was found in the plasma but was lower than that reported in rats and *macaca nemestrina*. No lipophilic radiolabelled metabolites were found in human plasma.

They concluded that there was a rapid uptake of ^{11}C-SCH442416 and that it was observed in all regions of the brain reaching a maximum at approximately 3 minutes. The results from the spectral analysis indicated that the various components can be separated into irreversible nonspecific binding, reversible nonspecific binding, reversible specific binding and a blood component. In addition, the binding potentials of the non-displaceable binding BP_{ND} were calculated using cerebellar volume of distribution. This was an estimate of the reversible non-displaceable binding across the entire brain and gave the following mean binding potentials BP_{ND}: 2.5 (putamen), 1.6 (caudate) and 0.5 (thalamus).

http://dx.doi.org/10.17229/jdit.2015-0202-011

ISSN: 2057-3782

PET Imaging

In the second article, *'An in vivo Positron Emission Tomography Study of Adenosine 2A Receptor Occupancy by Preladenant using ^{11}C-SCH442416 in Healthy Subjects'*, by Grachev *et al*: a PET study was carried out to investigate the receptor occupancy of ^{11}C-SCH442416 in the human brain. The aim of this study was to determine the plasma concentration and dose of ^{11}C-SCH442416 required for the management of Parkinson's disease. A patient group of 18 people was involved in the PET study who each received an intravenous injection of the radiotracer ^{11}C-SCH442416. A total of 13 patients received a single dose of preladenant with strengths of 10, 50 or 200 mg to be taken orally at 1, 6 or 12 hour intervals prior to the injection of the radiotracer.

The PET imaging results indicated that the 50-200 mg doses of preladenant provided a blockade effect greater than 80%. A dose of 5 mg twice daily of preladenant, was estimated to provide ≥50% receptor occupancy - in approximately 75% of the patient population - for the majority of the waking hours, which amounted to 12 hours daily.

The authors concluded that single doses of preladenant were well-tolerated and the C_{max} and AUC values of preladenant increased according to dosage given. This study demonstrated the importance of PET imaging for establishing PK-PD relationships and in addition provided the tools for confirming proof-of-target and dose guidance for Phase 2/3 clinical trials.

Automated Radiosynthesis

In the following article, '*Automated synthesis of [^{18}F]fluorocholine using a modified GE TracerLab module'* by Mansi *et al;* the authors made modifications to the reactor design in the GE TracerLab FX(FDG) module. This was to be utilised in the automated radiosynthesis of [^{18}F]fluorocholine. This PET tracer was synthesized in two steps and the new reactor design produced high radiochemical purity and reproducible yields of [^{18}F]fluorocholine. Consequently, this automated approach can be applied to routine PET imaging of various oncological disease states observed in the clinical setting.

^{18}F-FES-PET/CT Imaging

In the article entitled, *'[^{18}F]-Estradiol PET/CT Imaging in Breast Cancer Patients'* by Vaalavirta *et al.*, the authors demonstrated - in their preliminary work - that tumor imaging with 16α-[^{18}F]-fluoro-17β-estradiol (^{18}F-FES) could be useful in the determination of the status of estrogen receptor (ER) and in the prognosis of hormonal therapy for breast cancer patients. The authors suggest potential scenarios whereby this functional metabolic imaging could be considered in the clinical setting for guiding ER-positive breast cancer treatment in difficult individual cases.

The study group included 18 breast cancer patients, 17 of whom were subjected to a PET-CT scan using the radiotracer ^{18}F-FES. The follow up of the patients involved using hormonal therapy, radiation therapy or chemotherapy. The study of this patient group revealed 148 metastatic lesions from the ^{18}F-FES-PET/CT imaging. These lesions were located in primary tumour, lymph nodes, lungs and bones.

In conclusion, the authors found a reasonable correlation between SUV_{max} of lesions on ^{18}F-FES-PET/CT and using the tumour marker carcinoembryonic antigen (CEA). The tracer ^{18}F-FES has demonstrated to be a promising *in vivo* imaging agent for ER status of primary and metastatic breast

cancer. The application of PET-CT using estradiol, labelled with fluorine-18 has the ability to be an important diagnostic tool in the assessment of hormone-dependent breast cancer.

Prostate Cancer Therapy

Subsequently, in this case study entitled, '*Abiraterone and Volumetric Modulated Arc Therapy for Second Recurrence of Node-Positive Prostate Cancer - A Case Report'* by von Eyben *et al;* the authors reviewed the treatment of a 50 year old man with prostate cancer. This man was initially treated with radical prostatectomy and pelvic lymph node dissection. He had salvage androgen deprivation therapy (ADT) for persistent measurable prostate specific antigen (PSA).

The first recurrence in 2011 was treated with volumetric modulated arc therapy (VMAT). However in 2014, an ^{11}C-choline PET/CT scan indicated a second recurrence with new lesions in two para-aortal lymph nodes. Abiraterone (Zytiga®) gave a fall of PSA from 2.9 to 0.54 ng/mL, over a four month period. Following this, a para-aortal lymph node lesion was given VMAT with a boost of 60 Gy. The treatment was well tolerated by the patient.

Tumour Imaging

Furthermore, the review article, *'^{68}Ga-Somatostatin analogue PET-CT in neuroendocrine / tumours*' by Giovannini *et al.* This review was based on a PubMed search of medical literature and reflects the systems of classification, grading and staging of neuroendocrine tumours (NETs).

The review also focused on the management of patients with NETs, in particular the role of ^{68}Ga-DOTA-SSTRTs PET/CT imaging. Neuroendocrine tumours (NETs) included a spectrum of neoplasms characterized by histologic heterogeneity - with significant clinical differences. NETs are well differentiated tumours but often present metastases at diagnosis and therefore conventional imaging techniques create results which are insufficient for early diagnosis and therapy monitoring.

The standardized morphological criteria to assess treatment response are inadequate in NETs, because of their biologic evolution and the cytostatic nature of new oncologic treatments. Functional imaging modalities have improved the understanding and diagnosis of NETs by the use of somatostatin analogue tracers labelled with radioisotopes.

^{111}In-Octreotide scintigraphy was considered the gold standard imaging modality for NET detection with diagnostic accuracy of approximately 90%. However, ^{68}Ga-Dota-SST radiotracers (SSTRTs) PET/CT represent a superior imaging procedure with higher accuracy for detection of NET lesions, as compared to morphological imaging procedures and somatostatin receptor scintigraphy.

Therefore, the use of somatostatin analogue radiolabelled tracers offers the possibility to non-invasively evaluate the presence of somatostatin receptor expression on NET cells, with direct therapeutic implications.

Targeted Radionuclide Therapy

In this article Dr. Eckelman comments on '*Targeted radionuclide therapy and its potential role in nuclear medicine*' and draws a parallel with [^{131}I]iodide for the treatment of thyroid abnormalities. This paradigm shift from predominately technical advances requires radioligands, designed to have a significant impact on the present standard of care. However, this shift is especially challenging for

ISSN: 2057-3782

diagnosis or staging in the areas of neurology, psychiatry and cardiology. This extends to challenges in oncology and infectious disease cases.

A validated single scan approach for diagnostics is also critical to the success of Nuclear Medicine. Choosing a high affinity target for radionuclide therapy- that is highly expressed through the disease stages - is likewise challenging. In this paradigm shift, investigators require a clear understanding of whether the goal is monitoring the change in target - as a function of disease and treatment - or if the goal is to detect as many abnormalities as possible, as a function of disease or treatment. With these goals in mind, choosing a target for radionuclide therapy which uses biomarkers/diagnostics to personalize treatment has the potential to increase the impact of targeted Nuclear Medicine.

Ultrasound Imaging

The next paper entitled, '*Update on transcranial sonography applications in movement disorders'*, by Godani *et al*; reviews the literature on transcranial B-mode sonography (TCS) of brain parenchyma and is increasingly being used as a diagnostic tool for disorders of movement. The most widely recognized finding for movement disorders has been an increase in echogenicity of the substantia nigra: an area of the midbrain that is affected by idiopathic Parkinson's disease (IPD).

This finding has enabled the reliable diagnosis of IPD, with high predictive values. Other sonographic features, such as hypoechogenicity of the brainstem raphe and hyperechogenicity of the lentiform nucleus, might aid the differential diagnosis of IPD amongst other movement disorders. In comparison to other neuroimaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT); TCS can be performed currently by the use of portable machines and has the dual advantages of being non-invasive and also highly resistant to movement artifacts. In certain brain disorders, TCS detects abnormalities that cannot be visualized or can only be visualized with extreme effort with alternative imaging methods.

This update summarizes the current methodological standards and defines the assessment of diagnostically relevant deep brain structures such as substantia nigra, brainstem raphe, basal ganglia and ventricles for differential diagnosis of IPD and other movement disorders. Finally, the authors have provided detailed information about the advantages and limitations of this novel neuroimaging method.

Atheroma PET Imaging

In the penultimate paper by Strauss *et al*, entitled, '*^{18}F-Fluoride as a marker of unstable atheroma – A Perspective'*; describes techniques currently available to detect myocardial and cerebral ischemia and identify patients with advanced atherosclerosis. The localization and characterization of atheroma prior to a clinical event allows therapeutic intervention before any loss of function due to ischemia or infarction.

To enable a high level of specificity, the imaging technique should highlight lesions with potential to cause a clinical diagnosis. Several radiopharmaceuticals have been described to identify inflamed, thin-cap atheroma; of these, the ionic fluoride ion (^{18}F-) may be the most useful. Preliminary

ISSN: 2057-3782

studies suggest that ^{18}F- does not usually localize in areas of dense vascular calcification but does form in locations of microcalcification.

Although the local pathophysiology required for fluoride localization is not fully understood, it appears that localization occurs in regions of severe inflammation. The lack of significant uptake in normal myocardium or normal brain, suggest that low levels of fluoride uptake should provide a sufficient signal to detect small lesions. Although more work is needed to develop standard methods of quantitation and image mapping; ^{18}F-PET-CT imaging may be useful in identifying vulnerable cases of atheroma.

Molecular Imaging and Radionuclide Therapy

The final paper in the inaugural issue entitled, *'Basic premises to molecular imaging and radionuclide therapy. Journal of Diagnostic Imaging in Therapy'*, by Mansi *et al* includes a complementary article attached to an accompanying paper which will be included in a forthcoming issue. The aim is to provide an overview synopsis on the central role of chelation in labelling radiocompounds for radionuclide therapy and/or imaging purposes.

In order to maintain a deeper understanding of the importance of '*Chelator-Based Imaging & Therapy'* which the authors have briefly discussed in this current issue – it was intended to provide a brief introduction to the contents included within the second paper; which will contain the most significant principles of molecular imaging and radionuclide therapy.

Accordingly, whilst the chelation process is of utmost importance to the Nuclear Medicine community, the aim is to highlight examples of the chelation processes, especially labelling with radiometals and to contain the various categories of radionuclides currently available.

Overall commercially the synthesis of many of these novel 'radiotherapeutic bullets' involve some interesting biopharmaceuticals. The technological drive is to produce the radiopharmaceuticals that can be labelled with beta emitters and the more effective – less manageable - alpha emitters. Consequently, the radiochemistry of the radio-halogens such as radioiodine and fluorine-18 will play a crucial role in future development of these radiopharmaceutical bullets.

In accordance with radiolabelling using chelates the interest in radiometals will similarly increase and be pivotal in diagnostic and/or therapeutic purposes in the clinical setting.

Furthermore, the advancement of chemical synthesis will afford the development of significant PET imaging agents surpassing ^{18}FDG with the individualization of new radiochelates having the capability to increase the boundaries currently occupied by SPECT and evolve novel applications in molecular imaging.

Going forward

This new journal has captured the imagination of many scientists working in nuclear medicine, diagnostics, imaging and therapy. The journal owes its success to a number of authors who have submitted high quality manuscripts and shared their in-depth knowledge in the areas of diagnostic imaging and therapy. One focus of the journal is to give a clinical overview of a selections of articles. This journal will support the public interest of science literature by using an innovative process which reduces the time of publication and increases the quality of the review process.

http://dx.doi.org/10.17229/jdit.2015-0202-011

ISSN: 2057-3782

The JDIT peer-review process is coordinated by the Open Access Scientist who will complete an initial assessment of your article within 3 days of submission. If successful, the article will enter the peer-review process, which should be completed within 28 days, leading to a successful e-publication.

Open Medscience is designed to offer a cross-media platform to take into account the technological advances in mobile devices. This approach to the website design will make the submission and/or publication of JDIT articles more accessible and user friendly. Open Medscience will share your article on social media platforms.

The idea behind thematic issues is to generate maximum impact of the published subject matter in the particular area of radiopharmaceuticals thereby increasing the journals' impact factor. Finally, we have some very interesting articles and reviews, which will be published in forthcoming issues. JDIT is growing rapidly and consequently its reputation amongst academic researchers and pharmaceutical companies, institutions and universities is being enhanced.

Prof. Andrea Ciarmiello
Editor-in-Chief
Journal of Diagnostic Imaging in Therapy

Prof. Luigi Mansi
Co-Editor-in-Chief:
Journal of Diagnostic Imaging in Therapy

Inaugural Issue - Table of Contents

[5] von Eyben FE, Joensuu T, Kangasmaki A, Kairemo K, Kiljunen T. Abiraterone and Volumetric Modulated Arc Therapy for Second Recurrence of Node-Positive Prostate Cancer - A Case Report. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 73-80. [CrossRef]

[6] Giovannini E, Gaeta M, Ciarmiello A. ^{68}Ga-Somatostatin analogue PET/CT in neuroendocrine tumors. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 81-102. [CrossRef]

[7] Eckelman WC. Choosing a target for targeted radionuclide therapy using biomarkers to personalize treatment. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 103-109. [CrossRef]

[8] Godani M, Canavese F, Del Sette M, Walter U. Update on transcranial sonography applications in movement disorders. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 110-128. [CrossRef]

[9] Strauss HW, Mariani G, Volterrani D. ^{18}F-Fluoride as a marker of unstable atheroma – A Perspective. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 129-136. [CrossRef]

[10] Mansi L, Kitson SL, Cuccurullo V, Ciarmiello A. Basic premises to molecular imaging and radionuclide therapy. *Journal of Diagnostic Imaging in Therapy*. 2014; 1(1): 137-156. [CrossRef]

Citation: Ciarmiello A, Mansi L. Inaugural Editorial Review - Nuclear Medicine, Diagnostic Imaging and Therapy. *Journal of Diagnostic Imaging in Therapy*. 2015; 2(1): 1-8.

DOI: http://dx.doi.org/10.17229/jdit.2015-0202-011

Published Online 02 February 2015 http://www.openmedscience.com