Clin Transl Imaging (2014) 2:183–185
DOI 10.1007/s40336-014-0065-z

GUEST EDITORIAL

Trends in PET quantification: opportunities and challenges

Habib Zaidi · Abass Alavi

Received: 6 May 2014 / Accepted: 10 May 2014 / Published online: 4 June 2014
© Italian Association of Nuclear Medicine and Molecular Imaging 2014

Since its inception, positron emission tomography (PET) has emerged as a non-invasive imaging modality that allows, in different fields (neurology, cardiology and oncology), in vivo quantitative assessment of molecular and physiological biomarkers in healthy and disease states [1–4]. Quantitative analysis makes it possible to establish a direct relationship between the time-varying activity concentration in organs/tissues of interest and the functional parameters representing the underlying biological processes at the cellular level [5–8]. It should, however, be emphasized that the term quantification has often been used inappropriately in the medical imaging literature to indicate different measurement approaches such as [5]: (1) semi-quantification (a contradiction in terms) or relative quantification (e.g., measurement of SUV), (2) absolute quantification of activity concentration, usually incorporating careful corrections for physical degrading factors (e.g., measurement of tracer uptake in MBq), and (3) proper physiological quantification, where the absolute activity concentration [obtained in (2)] is converted into molecular parameters of interest [e.g., glucose metabolic rate (rGMCglc) expressed as mol/100 g/min].

The concentration of tracers in organs/tissues of interest depends on their specific kinetic properties, i.e., various factors including, but not limited to, the rate of delivery through circulation, the biochemical reactions involved in the specific biological process under examination, biological clearance, and so on. Furthermore, the measurement of radioactivity in volumes of interest must take into account the physical half-life of the radionuclide employed for the pharmaceutical labeling. These physiological and physical factors must be fully taken into consideration if quantitative PET is to realize its full potential, and thus allow assessment of the physiological and molecular characteristics of the cells and organs/tissues under examination. Using these approaches, it is possible to quantify a number of processes, including the rate of glucose utilization, receptor binding, receptor occupancy, and so on. The resulting estimates can then be linked to clinical outcomes (e.g., disease evolution, response to treatment, survival) so that disease activity can be assessed and related to the underlying pathological states. Moreover, these quantitative measures can provide surrogate endpoints in therapy trials.

The major challenges to quantitative preclinical PET imaging, when the aim is to quantify biological or pharmacokinetic processes, can be categorized in five classes [9, 10]:

- Instrumentation and measurement factors: factors related to imaging system performance and data acquisition protocols;
- Physical factors: those related to the physics of photon interaction with biological tissues;

H. Zaidi (✉)
Division of Nuclear Medicine and Molecular Imaging, Geneva University Hospital, 1211 Geneva, Switzerland
e-mail: Habib.Zaidi@hcuge.ch

H. Zaidi
Geneva Neuroscience Center, Geneva University, 1205 Geneva, Switzerland

H. Zaidi
Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, 9700 RB Groningen, The Netherlands

A. Alavi
Division of Research, Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

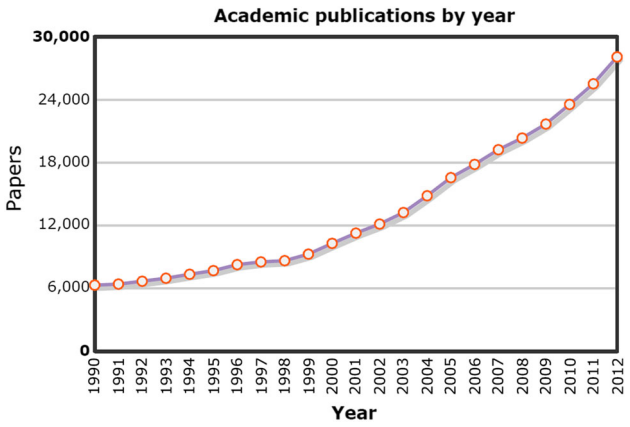

Fig. 1 The increasing number of annual peer-reviewed publications (between 1990 and 2012) reporting on developments in or use of PET quantification demonstrates the growing interest in this area. This graph is based on a PubMed query with the following mesh terms: "PET" or "Positron emission tomography" and "quantification" or "quantitation" or "quantitative". A time line was created with MEDSUM: an online MEDLINE summary tool by Galsworthy, MJ. Hosted by the Institute of Biomedical Informatics (IBMI), Faculty of Medicine, University of Ljubljana, Slovenia (www.medsum.info) (Color figure online at http://link.springer.com/article/10.1007/s40336-014-0065-z)

- Reconstruction factors: issues related to assumptions made by image reconstruction algorithms;
- Physiological factors: factors related to motion and physiological issues including blood flow;
- Tracer kinetic factors: issues related to difficulties in developing and applying tracer kinetic models, especially at the voxel level (parametric imaging).

Both the present and the forthcoming issue of *Clinical and Translational Imaging* examine in depth the challenges to optimal quantification relating to these essential factors.

Utilization of quantitative PET imaging is expected to increase with the development of specific targeted molecular imaging probes. Accurate quantitative methods are needed so that these might be adopted as validated approaches in various clinical settings. A PubMed search dating back to 1990 and conducted using the query "PET" or "Positron emission tomography" and "quantification" or "quantitation" or "quantitative" (Fig. 1) yielded more than 310,575 entries. Although this result does not equate with 310,575 papers dealing specifically with PET quantification, the exponential increase in the occurrence of these words is an indicator that quantitative molecular imaging with this evolving technology is a rapidly growing field (an increase of ~350 % from 1990 to 2012).

This is an exciting time for quantitative molecular imaging with PET. Recent decades have seen a steady increase in the number of published papers on this topic. This is why we have decided to devote two issues to trends in the dynamically changing field of PET quantification. The present issue looks at methodological developments, while the next issue will focus on clinical applications. The development of PET quantification has been very rapid and exciting, and there is every reason to believe that the field will move forward even more rapidly in the coming years with the advent of novel molecular imaging probes and new and innovative methodologies developed by the field's most creative researchers. Despite the remarkable achievements summarized in these issues and numerous other peer-reviewed journals, there is still a great deal left to be done in the years to come. There is no shortage of challenges and opportunities for quantitative PET imaging today. Despite the limited space available, we hope we have succeeded in giving the readers of this journal a real taste of recent developments in this field and of their potential applications in clinical and research settings in the future. Compiling these two issues has been, for us, a rewarding and instructive experience and we hope that our readers will find their contents of value in their respective disciplines.

Acknowledgments The Guest Editors are especially grateful to the authors who have contributed to these two special issues, as well as to the reviewers for their valuable comments and suggestions. They would also like to thank Catherine Wrenn for her skillful linguistic revision of the papers and Dr. Barbara Pedrotti (Springer-Verlag Italia) for her support and patience in bringing these issues to print.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Reivich M, Kuhl D, Wolf A, Greenberg J, Phelps M, Ido T et al (1979) The [^{18}F]fluorodeoxyglucose method for the measurement of local cerebral glucose utilization in man. Circ Res 44:127–137
2. Phelps ME, Huang SC, Hoffman EJ, Selin C, Sokoloff L, Kuhl DE (1979) Tomographic measurement of local cerebral glucose metabolic rate in humans with (F-18)2-fluoro-2-deoxy-D-glucose: validation of method. Ann Neurol 6:371–388
3. Wisenberg G, Schelbert HR, Hoffman EJ, Phelps ME, Robinson GD Jr, Selin CE et al (1981) In vivo quantitation of regional myocardial blood flow by positron-emission computed tomography. Circulation 63:1248–1258
4. Di Chiro G, DeLaPaz RL, Brooks RA, Sokoloff L, Kornblith PL, Smith BH et al (1982) Glucose utilization of cerebral gliomas measured by [^{18}F] fluorodeoxyglucose and positron emission tomography. Neurology 32:1323–1329
5. Zaidi H (ed) (2006) Quantitative analysis in nuclear medicine imaging. Springer, New York
6. Acton PD, Zhuang H, Alavi A (2004) Quantification in PET. Radiol Clin N Am 42:1055–1062
7. Boellaard R (2009) Standards for PET image acquisition and quantitative data analysis. J Nucl Med 50:11S–20S
8. Rosenthal MS, Cullom J, Hawkins W, Moore SC, Tsui BM, Yester M (1995) Quantitative SPECT imaging: a review and recommendations by the Focus Committee of the Society of Nuclear Medicine Computer and Instrumentation Council. J Nucl Med 36:1489–1513

9. Zaidi H, Montandon M-L, Meikle S (2007) Strategies for attenuation compensation in neurological PET studies. Neuroimage 34:518–541

10. Zaidi H (2014) Quantification of small-animal imaging data. In: Zaidi H (ed) Molecular imaging of small animals: instrumentation and applications. Springer, New York, pp 467–494