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This Week's Citation Classic®

Hoffman E J, Huang S-C & Phelps M E. Quantitation in positron emission computed tomography: 1. Effect of object size. *J. Comput. Assist. Tomogr.* 3:299-308, 1979.
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The ability of a positron emission tomography camera to perform quantitative isotope concentration measurements, when the size of the object of interest was comparable to the resolution of the camera, was investigated. The experimental and theoretical relationship between object size and recovery of quantitative information for a given spatial resolution was established and methods to correct for errors due to poor resolution were suggested. [The *SCI*® indicates that this paper has been cited in over 230 publications.]

PET—A Noninvasive *In Vivo* Method

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In 1976 Michael E. Phelps, David E. Kuhl, and I came to the University of California, Los Angeles, to create a laboratory for the development and application of positron emission tomography (PET) for use as both a clinical and a basic biological research tool. Sung-Cheng Huang joined the group in 1977.

PET is unique among medical imaging modalities in that the image can provide an unambiguous and quantitative measure of isotope concentrations in tissue following injection of radiopharmaceuticals labeled with positron emitters. In X-ray computed tomography (CT) and magnetic resonance imaging (MRI), which produce superb images, the nature of the quantity being imaged is ambiguous, while in nuclear medicine, the fact that the instrument is unambiguously viewing isotope concentrations is not very useful because it is almost impossible to make the quantitative measurement. Because of this quantitative capacity of PET and the nature of radiolabeled compounds available, it is possible to use PET to perform noninvasive *in vivo* measurements in man of such quantities as blood flow and metabolism in the brain and heart.

Unfortunately, nothing is quite that simple. In 1977-1980 many investigators were using numbers from PET images as isotope concentrations without consideration of sources of background noise and the limitations of the technique due to its relatively poor spatial resolution. Resolution was normally viewed as the ability to see small objects or to distinguish close lying objects. A primary measure of radiographic resolution was the number of line pairs resolved per mm. Even sophisticated analysis of resolution in terms of spatial frequencies provided little practical insight on the effect of resolution on the measurement of isotope concentration from an image. The work that was presented in this paper showed the measured and theoretical relationship between object size and error of a PET measurement for a given resolution. On the positive side, this relationship could also be used to correct measurements when supplementary information about the dimensions of the structures of interest was available from other measurements, such as X-ray CT, ultrasound, or MRI. The paper also showed that with the typical PET resolutions of that day (ca. 18 x 18 x 18 mm^3), the isotope concentrations in most structures of an organ such as the brain were significantly underestimated (10-90 percent). Even today with resolutions of 6 mm (a factor of 27 smaller volume element), errors due to resolution effects are a constant concern in all PET measurements.

This work is highly cited because it addresses the most serious problem encountered in PET in any attempt to extract quantitative information, it provides a simple way to estimate the error, and it provides a method to compensate for the problem for some cases. It is also highly cited because we made the paper the first of a series of articles. When the paper was first submitted, Giovanni DiChiro, the editor, was hesitant in accepting the title, because all he had in hand was one paper. When he indicated his concern, we sent him outlines and abstracts of the next three parts of the series.[1-3] He decided to trust us to deliver at least one more part. There are now eight papers in the series,[1-6] two of which deal with other aspects of the resolution problem.[4,5] Of course each time someone comes across one of these papers, he or she is immediately aware of the existence of the rest of the series.

1. **Huang S-C, Hoffman E J, Phelps M E & Kuhl D E.** Quantitation in positron emission computed tomography: 2. Effects of inaccurate attenuation correction. *J. Comput. Assist. Tomogr.* 3:804-14, 1979. (Cited 85 times.)
2. ————. Quantitation in positron emission computed tomography: 3. Effect of sampling. *J. Comput. Assist. Tomogr.* 4:819-26, 1980. (Cited 35 times.)
3. **Hoffman E J, Huang S-C, Phelps M E & Kuhl D E.** Quantitation in positron emission computed tomography: 4. Effect of accidental coincidences. *J. Comput. Assist. Tomogr.* 5:391-400, 1981. (Cited 45 times.)
4. **Mazziotta J C, Phelps M E, Plummer D & Kuhl D E.** Quantitation in positron emission computed tomography: 5. Physical-anatomical effects. *J. Comput. Assist. Tomogr.* 5:734-43, 1981. (Cited 140 times.)
5. **Hoffman E J, Huang S-C, Plummer D & Phelps M E.** Quantitation in positron emission computed tomography: 6. Effect of nonuniform resolution. *J. Comput. Assist. Tomogr.* 6:987-99, 1982. (Cited 25 times.)
6. **Casey M E & Hoffman E J.** Quantitation in positron emission computed tomography: 7. A technique to reduce noise in accidental coincidence measurements and coincidence efficiency calibration. *J. Comput. Assist. Tomogr.* 10:845-50, 1986.

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