Overview of advances in imaging equipment in Nuclear Medicine / PET/CT

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Imaging of functional and metabolic processes in vivo, using pharmaceuticals labeled with isotopes which emit either single photons or positrons, has the major advantage of having the capability to detect disease ahead of the appearance of morphological tissue changes. The techniques of single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are limited by their poor spatial resolution and their inability to provide accurate localization. Sites of uptake can indicate disease or normal physiological distribution. Recent years have seen a significant expansion in the capability of Nuclear Medicine, largely through the introduction of PET and the development of Hybrid Imaging systems.

The principal cause of the observed poor image quality in SPECT imaging is attenuation. Combined SPECT/CT acquisitions provide an individual x-ray map of attenuation coefficients for each patient by sequential and near-simultaneous acquisitions with SPECT and CT. The resulting CT values are converted to account for the energy dependence of photon interaction with tissue, taking into account that the photon energies for SPECT and PET are different from the energy range of the x-rays in a CT system. In addition to the benefits of attenuation correction, the advantages of fused anatomical and functional images include improved lesion detection, more accurate localization of disease, and the characterization of small or unexpected lesions.

Incorporation of higher resolution CT imaging aids the elimination of the partial volume effects which result from the low spatial resolution of the SPECT/PET images. One of the most significant advances in nuclear medicine has been the development of iterative reconstruction algorithms, which can incorporate corrections for attenuation, scatter and partial volume effects. An iterative reconstruction algorithm compares a simulated measurement to the real image data and applies corrections until the two models agree. Methods applying Monte Carlo simulations are in development, as they can model a system very accurately and are the most precise method to compensate for isotopes which have multiple energy peaks and those resulting in bremsstrahlung. Due to the long times required for the computations these methods are not yet optimized for a clinical setting.

Improved detector crystals have been developed for gamma cameras with the advent of solid state detectors such as cadmium zinc telluride (CZT). This material has a much higher energy resolution when compared to NaI(Tl), which is important for rejecting scatter photons. These crystals can also be designed in a pixelated fashion, where the single NaI(Tl) crystal is replaced by an array of independent CZT crystals. This improves the count rate capability of the camera especially for high activities which would normally result in significant dead time.

PET has been described as the most important advance in biomedical science since the invention of the microscope. PET yields physiological information based on altered tissue metabolism by showing functional information on the processes in which the PET tracer is involved. The most important PET tracer is ^{18}FDG, which is concentrated in the tissues of high glucose metabolism such as primary tumors and their metastases. PET/CT and SPECT/CT are now widely used for the characterization of disease before and after treatment, and for the precise planning of biopsy and therapy procedures.

PET scanning has developed in several ways. Scanners have developed from operating in 2D to a 3D mode. In 2D annular septa are used in a similar way as parallel hole collimators in gamma cameras, and allow detection of only direct plane and cross-plane events. In 3D imaging, the septa are removed and coincidences are allowed for crystals pertaining to different rings. This increases the detection solid angle, and hence the scanner sensitivity is significantly improved. In order to produce images, the 3-D sinograms are re-binned into a set of 2-D equivalent projections. This may be done by assigning axially tilted lines of response to transaxial planes intersecting them at their axial midpoints (single slice rebinnning method or SSRB). In Fourier rebinning (FORE), the rebinning is performed by applying the Fourier method to each oblique sinogram in the frequency domain. This provides a more accurate estimate of the source axial location than was possible in SSRB. After rebinning of 3D into 2 D either filtered backprojection or an iterative method is applied to produce the final image. 3D mode has become more commonly used as the processing algorithms have increased in sophistication exploiting this modes inherently better sensitivity.

The first PET scanners used the same NaI crystals used in gamma cameras. Since then PET detectors have also been the focus of considerable development work. In order to work efficiently PET detectors must be smaller (in frontage), but thicker than detectors used in gamma cameras. BGO (bismuth germanate) crystals (which have a high density and atomic number) offered an effective solution and soon became the scintillator of choice. More recently scanners have been developed which use detectors based on crystals such as barium flouride and

gadolinium oxyorthosilicate. Cerium-doped letetium oxyorthosilicate has a very high density and rapidly converts annihilation photon energy into light. The combination of high light output and a short time constant allow for very fast timing (i.e. a short coincidence window), which reduces the chance of random coincidences and reduces the dead time. Faster detectors have been used in the development of Time of Flight scanners. Time of flight uses the time difference between the detection of coincident events to more accurately identify the origin of the annihilation. Time of flight scanners require detectors with ultra fast system timing resolution (~ 600 pico seconds for lutetium-yttrium oxyorthosilicate detector), but can considerably increase SNR, especially on wider FOVs.

PET & SPECT systems have been combined with a range of CT scanners. Early systems used basic CT scanners for localization and attenuation correction. These systems had the advantage lower patient doses. Modern scanners may be combined with fully diagnostic multislice CT systems. These enhance the imaging capability of the combined system but also add to the potential dose the patient may receive from the scan. For example a 400MBq FDG scan has a typical patient effective dose of 8mSv; A whole body localization CT scan may delver a further 1-5 mSv patient dose; a whole body diagnostic CT scan may add 15-25 mSv to the patient doses. PET CT centres must ensure that robust procures are in place to manage correct use of diagnostic and localization scans to keep patient doses ALARA. Although not generally available commercially as clinical scanners, PET systems have also been combined with MRI scanners which may develop additional imaging potential while controlling patient radiation dose. In order to address concerns about increasing patient doses due to the hybrid imaging systems, a number of low dose CT systems have been developed and combined with SPECT. These systems significantly reduce the radiation dose form the CT scan by lowering the applied current. While the images are not of diagnostic quality, they are sufficient for attenuation correction and anatomic correlation.

Because of the long duration of the whole body PET scans, and the mismatch in acquisition times for the CT and PET scans, respiratory motion can be a major challenge for accurate localization and quantification of PET-FDG images. Respiratory motion may cause the lesions in the lung to be smeared and the images to be blurred. As well as reduced image quality, quantification of FDG uptake is affected, with the motion producing a reduction of the measured standard uptake value. Breathing motion also causes misregistrion in fused PET-CT images. Motion artifacts are a particular challenge for radiotherapy planning, and partly as a consequence of this limitation, CT remains the standard imaging method for treatment planning. Respiratory gating techniques have been developed which reduce motion artifacts by gating PET images in correlation with the respiration cycle. Some papers have shown that respiratory gating can improve target localization, and in radiotherapy permit reduction of tumor margins with a consequent reduction in the volume of normal tissue irradiated. This may allow further dose escalation to the target volume, and more normal tissue sparing.

Some of the low-dose CT (used in SPECT) can acquire the CT localization data over a longer time (>10s), resulting in blurring in the CT images which is comparable to that caused by the motion in the emission images. This can result in better registration between the images from the two modalities, but the image quality, localization (and quantitative analysis) will still be affected by motion blurring.

Radioisotopes are the basis of nuclear medicine imaging. A novel development in radionuclide therapy imaging with SPECT is bremsstrahlung imaging. In the case of therapy using a pure beta emitter (e.g. ^{90}Y,^{32}P) , imaging can be performed using the bremsstrahlung created as the beta particles lose energy in tissue. Cyclotron produced isotopes can provide alternatives to standard nuclear medicine scans. For example ^{18}F Sodium fluoride may be used for bone scans and with the current shortage of ^{99}Mo, may offer a feasible alternative for centers with PET scanning capability.

Clinical imaging in PET is largely based on ^{18}F FDG, which has a half life of approximately 110 minutes. Isotopes such as ^{15}O and ^{11}C have not achieved widespread clinical use, largely because of the practical limitation associated with their much shorter half lives. The high cost of installing and running a Cyclotron places a limit on the proliferation of PET scanning technology, as PET scanners must be located within a few hours travel of a cyclotron. This limitation is particularly evident in the uneven geographical distribution of cyclotrons, with approximately 80% of systems being based in Europe and United States. With the increased demand for PET scans work has also been undertaken on other mechanisms for generating isotopes. One intriguing possibility is a ‘bench-top’ version of a cyclotron. Although such a system would have a much lower yield than the standard medical cyclotron, its much smaller size may make it a more practical solution for some centers. These cyclotrons may also offer the possibility of producing other isotopes (e.g. ^{11}C) which could further develop the clinical applications in PET imaging.

Nuclear medicine / PET imaging modalities are constantly developing with improvements in detector materials, data acquisition and image processing technology. The combination of functional and anatomical information, together with the development of more sophisticated tracers brings Nuclear Medicine Imaging closer to being a clinical Molecular Imaging modality as the technology moves towards the visualization of pathological

processes at the cellular level.

Further reading

Principles and practice of Positron Emission Tomography, ed Wahl R, Lippincott Williams and Wilkins, 2002.

Nehmeh et al., Effect of respiratory gating on reducing lung motion artifacts in PET imaging of lung cancer, Medical Physics, Vol. 29, No. 3, March 2002.

Clinical PET, ED Schulthess G, Lippincott Williams and Wilkins, 2000.

IAEA Report 58, Radiation Protection in newer medical imaging technologies: PET/CT, 2008

Karp et al, Benefit of Time-of-Flight in PET: Experimental and Clinical Results, J Nucl Med 2008; 49:462–470.

Hybrid Imaging Technology: From Dreams and Vision to Clinical Devices, Patten et al, SNM, 2009.

Hybrid Imaging (SPECT/CT and PET/CT): Improving Therapeutic Decisions, Delbeke et al, SNM 2009.

Advances in SPECT imaging with respect to radionuclide therapy, QJ Nucl Med Mol Imag, D'Asseler, 2009.