# AAPM 2009 Annual Meeting
# Therapy Continuum Education Course
# TU-B-BRC-01 Handout

# Promise and Challenges of PET for Target Definition and Treatment Response Evaluation

## Part II
## Instrumental Accuracy and Challenges of PET

**Assen S Kirov, Ph.D.**
**Department of Medical Physics**
**Memorial Sloan-Kettering Cancer Center**
**New York**

**Tuesday, July 28, 2009**
**8:30 am, Room: Ballroom C**

## I. What can PET provide to RTP?

PET reveals functional information about elevated cell metabolic activity including prolifiteration, which may help localize the most active as well as the potentially radiation resistant parts of a tumor, as well as cancerous metabolic activity outside the CT drawn tumor volume (Fig.1 and Fig.2).

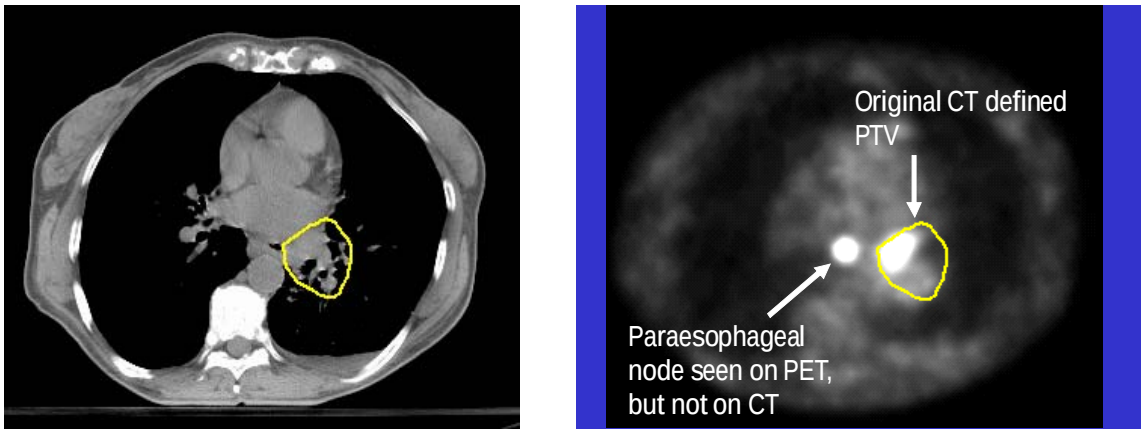


Fig.1. Registered CT (left) and PET images (right) of a mediastinal lung lesion.

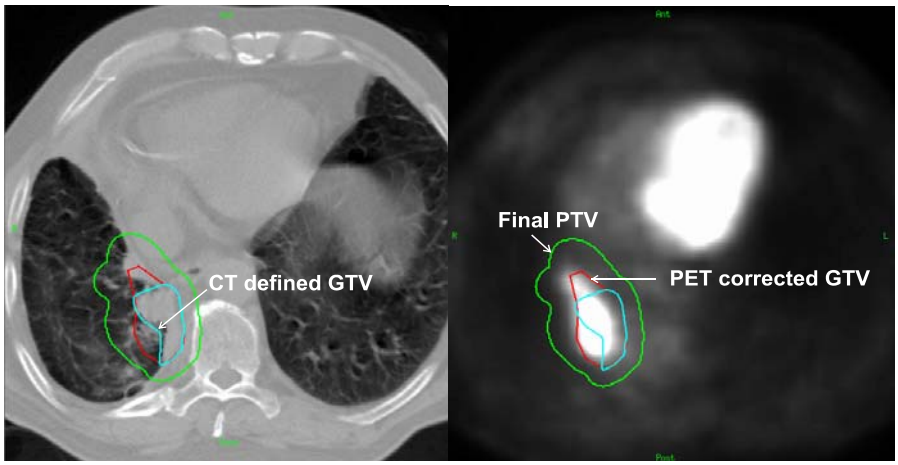


Fig.2. Example of modification of the Gross Tumor Volume contour (GTV) by PET

## II. What are the main instrumental PET image degrading factors and how are they corrected or accounted for?

The activity distribution in a PET image differs from the actual tracer activity distribution due to physical limitations of the PET scanners, which are described in Table 1 and elsewhere[2, 3]. We limit this lecture in describing the effects of some of these artifacts: namely attenuation correction, scatter and random events corrections and scanner resolution. Tumor motion is also one of the largest artifacts, but it will be only briefly described, since it has been the subject of other lectures.

An illustration of some of the physical phenomena based on a realistic Monte Carlo simulation of a PET scan is given in Fig.3.

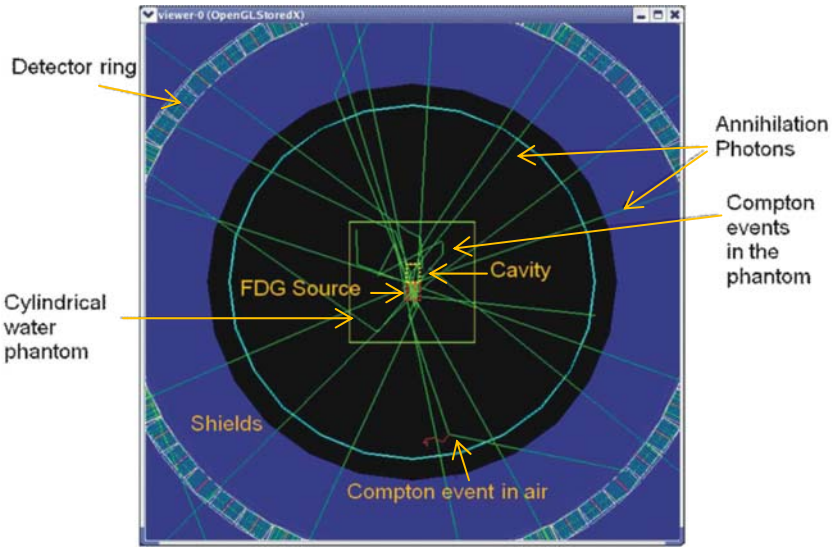


Fig.3. Visualization of a Monte Carlo simulation using GATE [1] of the photon trajectories (green lines) in a PET scanner. Compton scatter interactions in the water phantom (a water cylinder marked with yellow contour) can be seen. One of the Compton interactions occurs in air (a rare event, in which the knocked off electron has sufficiently long trajectory to be visible in red) after which the scattered photon is detected in the scanner ring.

Table 1. PET Image Degrading Factors

| No. | Factor | Brief description |
|---|---|---|
| 1 | PET resolution | Smearing of the activity concentration obtained with PET due to physical and detector phenomena (see Table 2.) |
| 2 | Photon Attenuation | Loss of photons emitted from the patient due to scatter or absorption in the human tissues |
| 3 | Photon Scatter | Deviation of photons from their original trajectory due to scatter. This may result in coincidences, which provide inaccurate “line of response” (or LOR, the line between the detectors hit by the 2 photons). |
| 4 | Random coincidences | Accidental coincidences from photons originating from the decay of different atomic nuclei. |
| 5 | Arc effects | For lines of response (see 3 above) close to the periphery of a PET scanner the effective detector face is less due to the curvature of the detector ring. |
| 6 | Limited Statistics | The limited statistics of the images makes image noise a problem, which is still under investigation. The dependence of the noise with activity depends on the reconstruction method used. |
| 7 | Electronics Dead Time | Loss of counts due to overloading with too many events of the electronic modules of the scanner. |
| 8 | Image Reconstruction | Mathematical operations on the PET data containing coincidences recorded along all lines of response from a PET scan, which return the activity distribution in the patient. |
| 9 | Registration with the attenuation image | The distribution of the attenuation properties inside the patient (i.e. bones vs. lung) needs to be aligned (ie, registered) accurately with the PET scan data. |
| 10 | Motion | Movement of the tumor and of neighboring tissues due to patient or organ motion. |

*Attenuation correction*

The attenuation correction (AC) may cause inaccuracies [4]:

(i) close to metallic implants (due to wrong CT numbers caused by CT streaking artifacts) resulting in overestimated attenuation which results in elevated activity;

(ii) due to motion resulting in loss of registration between the CT and PET images (see below)

(iii) due to use of contrast media, which may cause overestimation of the AC especially for older bilinear AC algorithms [5].

(iv) due to truncation – for large or mis-positioned patients, part of the patient may be outside the CT Field of View (FOV). Unaccounted attenuation results in underestimation of the SUV and will produce artifacts at the edge of the CT images – a rim of high activity at the edge of the CT FOV [4].

Dual energy CT attenuation correction methods have been proposed for reducing (iii) above [6].

*Respiratory motion*

The loss of registration between the CT and PET images can be corrected by building separate PET images for each breathing phase by assigning a phase to each recorded coincidence and by using a CT image for the same breathing phase. This method is known as 4D PET/CT[7]. Another method, the deep inspiration breath hold technique as well as a description of the different motion tracking devices are summarized in a recent review [8].

*Scatter corrections*

Various methods for evaluating the number of scatter events exist [2, 9] and can be performed at different levels of accuracy: uniform, in which the number of scattered photons across the sinogram is approximated by a smooth function, or more detailed and based on the attenuation correction (AC) image. Vendors apply the corrections so that they are generally seamless for the user. Calculating the scatter from the AC image was initiated by Olinger [10] and can be performed either analytically using the Klein-Nishina formula for single scattered photons, which is becoming the standard, or using Monte Carlo. The latter is a more accurate method, but very time consuming and currently different groups are working on improving the efficiency of such calculations.

*Random corrections*

The number of random events increases with increasing the injected activity. The random correction is obtained in one of the following three ways: (i) real time subtraction of the count rate from a delayed timing window for which no true coincidences are possible, (ii) off-line correction using a low-noise estimate of the randoms rate obtained by smoothing the delayed sinogram; or (iii) random rates calculated from the singles rate in each detector. Direct subtraction of real time measured random coincidences rate increases noise in the corrected image. Brasse et al [11] have shown that while smoothed random estimates provide the lowest noise images, singles-based random estimates perform only marginally worse, but are most time efficient and can lead to reduction of patient scan time.

*PET resolution*

Finite scanner resolution can prevent quantification and can even make invisible objects in PET if they are comparable or smaller than the Full Width at Half Maximum (FWHM). It can also lead to loss of quantitative accuracy for hot and cold spot recovery coefficients for larger objects. The effect is known as partial volume effect (PVE). The factors affecting PET resolution are listed in Table 2 and are described in detail in [3].

Table 2. Main factors affecting PET resolution.

| Number | Factor | Comment |
|---|---|---|
| 1 | Positron range | The distance the positron travels prior to annihilation, usually < 3 mm. It is ~ 0.6 mm for Fluor - 18, the radioactive isotope which is used most often. |
| 2 | Detector size and distance to detector | The PET spatial resolution usually can not be less than half the size of the face of the detector elements. Increasing the diameter of the detector rings improves resolution, but decreases sensitivity and increases the photon non-colinearity effect. |
| 3 | Photon non-colinearity | Since the positron is not fully stopped at the time of annihilation with an electron, the photons are not emitted exactly back-to-back. |
| 4 | Block effect | Scattering of photons in neighboring detectors will broaden the resolution. Also the block readout scheme can affect it. |
| 5 | Depth of interaction | The photons may protrude one detector without interaction and interact with a neighboring detector. |
| 6 | Under-sampling | In addition to the finite detector size, the angular sampling interval and the selected voxel size also impose a limit on the resolution. |
| 7 | Reconstruction | Smoothing functions are applied to the data during or post-reconstruction to suppress noise in the data. |

Various PVE correction methods exist, which apply the correction either at a region or at a voxel level [12], during or post reconstruction. Most of the correction methods lead to increase of noise in the image and use anatomical information to control it, except two recent approaches, which do not rely on additional anatomical (CT or MRI) images [13-15]. Fig.4 shows PET images before and after applying the second of these approaches.

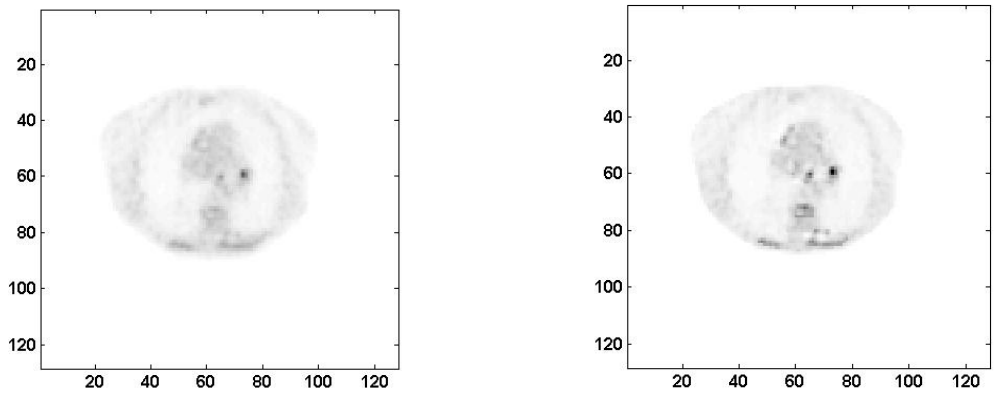


Fig.4. PET images before (left) and after (right) applying a partial volume effect correction [14].

However, these methods need further investigation and validation and should not be used in clinical practice until this is accomplished.

*PET reconstruction*

The selection of the reconstruction algorithm may affect the image quality as well as the Standard Uptake Value (SUV). Both filtered back-projection with re-projection and the iterative methods require smoothing to suppress variance, which affects resolution. The selection of reconstruction method and type of attenuation correction were shown to have an effect on the SUV [16]. It was also shown that the type of reconstruction algorithm and type of smoothing filter selected affect the capabilities of certain fixed threshold segmentation methods to segment accurately different size spheres in phantom [17, 18].

*Normalization correction*

Corrects for the "non-uniformity of detector response related to the geometry of the scanner" and for the difference in sensitivity between the different detector channels [9]. It is performed during routine re-calibration of the scanner by using a uniform activity cylinder or by a scanning rod source. The source and the correction procedures are specified by the vendor of the scanner. For more information on the different approaches for normalization correction see [19].

*Noise*

Riedel *et al*, [20] have shown high uniformity of the noise across FBP reconstructed images, which is somewhat reduced by the attenuation correction They have also shown that OSEM reconstruction leads to better signal to noise ratio (SNR) for low uptake lesions while FBP leads to better SNR for high uptake lesions. An investigation of the uncertainty introduced by noise in the images is investigated also in a poster SU-DD-A4-01 of this meeting.

*Dead time*

Corrections are needed to account for count loses due to the electronics dead time. Since the losses are larger at high count rates, this can be done by repetitive scans of a decaying source. High count rates can lead also to event mis-positioning due to pulse pile-up in block detector systems [19]. This may cause loss of imaging accuracy, if normalization is performed at count rates very different from these in clinical scans.

*Overall PET inaccuracy*

The overall quantification inaccuracy of PET scans is known for simple phantoms, but is not well studied for realistic cases, in which it is a complex superposition of the perturbing effect of the above phenomena. In a Monte Carlo based investigation we have showen how the different corrections and reconstruction algorithms will affect accuracy for the case of non-uniform activity and attenuation varying in one direction (Fig. 5.)[21].

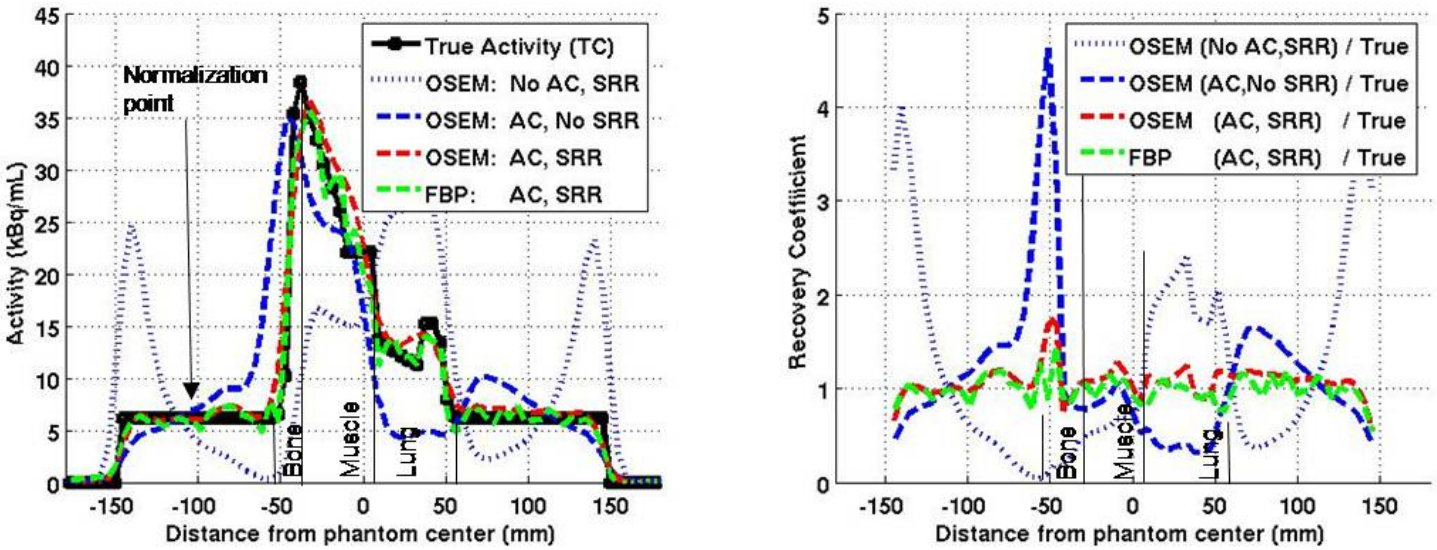


Fig.5. Activity profiles (left) and recovery coefficients (=recovered/true activity, right) across a 12 cm cubical phantom, in which the activity and the attenuation vary from left to right as indicated, inserted in a 30 cm diameter water cylinder with constant activity. The profiles are normalized at the indicated point in the background region. The notations are: OSEM = Ordered Subsets Expectation Maximization reconstruction algorithm, FBP = 3D Re-projection Filtered Back-Projection reconstruction algorithm, AC = attenuation correction, SRR = Scatter and Random Rejection.[21]

In poster SU-FF-I-147 by Kang *et al,* of this meeting are shown results of a MC investigation of the inaccuracy of PET also for patient specific activity and attenuation distribution. Through separation of the scatter and random events from the true it was shown that a given inaccuracy of the scatter corrections may lead to similar magnitude inaccuracy of the PET determined activity in part of the images. Simulations also allow investigating the effects of motion. One can introduce a known misalignment between the CT AC and PET at the reconstruction step. For a hypothetical patient shift for example of 1.5 cm, quantification errors close to 150% are seen in parts of the images.

## III. Challenges for PET based tumor segmentation

To segment a tumor form a PET image most current methods use a threshold either in SUV or in activity units, which is determined from scans of cylinders or spheres with known activity and in a known constant background activity. If used, it is particularly important to adapt the parameters in each of these methods to the scanner and protocol used in each institution. While some of these methods do provide a solid approach to the problem, they can not take into account the specifics of the activity distributions in patients. Tumors do not have symmetrical shapes and do not have uniform activity distribution either in the lesion or in the surrounding tissue, nor do patients have uniform attenuation properties. Significant differences between tumor volumes obtained with the various approaches have been found [22]. We have found that the variation between tumor volumes obtained with different methods (tested without adaptation to a specific scanner) is much larger for patients than for cylinders and spheres with uniform TC contained in a constant background [23]. Recently, new approaches emerged, which instead of activity or SUV thresholds use the activity gradient [24], region growing and active contours [25], or specifically account for the uncertainty and the imprecision in the images using fuzzy statistical models [26]. These methods show potential for more accurate segmentation of tumors with asymmetric shapes and non-uniform activity uptake.

Despite these developments, the segmentation of PET images is still a challenge since the quantitative accuracy of PET with respect to the underlying histopathology is limited. The quantitative accuracy of the PET image is affected by how well the selected tracer identifies the biological target and by the instrumental inaccuracies summarized in this handout. Resolution of each these two problems is needed to claim reliable and accurate tumor delineation.

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