SUV Analysis of F-18 FDG PET Imaging in the Vicinity of the Bladder

by

Colleen Marie Allen

Graduate Program in Medical Physics
Duke University

Date:_______________________

Approved:

___________________________
Timothy Turkington, Supervisor

___________________________
Terence Wong

___________________________
Shiva Das

Thesis submitted in partial fulfillment of
the requirements for the degree of Master of Science in the Graduate Program in
Medical Physics in the Graduate School
of Duke University

2012
ABSTRACT

SUV Analysis of F-18 FDG PET Imaging in the Vicinity of the Bladder

by

Colleen Marie Allen

Graduate Program in Medical Physics
Duke University

Date:_______________________

Approved:

___________________________
Timothy Turkington, Supervisor

___________________________
Terence Wong

___________________________
Shiva Das

An abstract of a thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University

2012
Abstract

Positron Emission Tomography with $^{18}$F-FDG can be used as a predictor for post-therapeutic tumor response in rectal and gynecologic cancers. An issue with assessing lesions in the vicinity of the bladder is the radioactivity that accumulates in the bladder due to constant filling. SUV analysis is used to discriminate between therapy responders and non-responders based on percentage change/threshold, but it is not yet known how much variability can be attributed to the bladder radioactivity. The purpose of this research is to understand the effects of bladder radioactivity on surrounding concentration measurements with different scanning and image reconstruction techniques.

Methods: ROI analysis was performed on 67 PET scans from DUMC. Typical values of bladder volume, radioactivity, radioactivity concentration and bladder-to-background uptake ratio were determined and incorporated into phantom studies. A bladder phantom insert was created for a 25 L torso phantom to explore effects of a bladder in the center of the FOV, on the edge of the FOV, and outside the FOV on the GE Discovery STE. The bladder insert was also used in a phantom study to assess the effects of different, realistic bladder radioactivity levels on surrounding 1-cm lesions on both the GE Discovery STE and GE Discovery 690. Background activity and in-air environments were explored, as well 2D, 3D and time-of-flight PET acquisitions with different image reconstruction techniques.
Results: The DSTE 2D PET data suffered large void artifacts that worsened as radioactivity in the bladder increased. The DSTE 3D PET data over-estimated background measurements up to 30 slices with the bladder outside the FOV. Concentration measurements within 4 cm distal to the bladder showed great variability and were generally recovered best with TOF PET or 3D PET with an increased number of iterations. Lesions greater than 4 cm distal to the bladder showed consistent recovery in both the 3D and TOF PET data.

Discussion: Radioactivity within the bladder has substantial effects on surrounding radioactivity concentration measurements. There are limits to the measurements of the radioactivity concentration values used in SUV analysis in the vicinity of the bladder. A general theme is that more accurate results are produced with smaller amounts of radioactivity in the bladder. This validates the DUMC protocol that begins acquisition just below the pelvic area to reduce as much filling as possible and highlights the usefulness of patient voiding prior to scanning.
Contents

Abstract ........................................................................................................................................iv

List of Figures .............................................................................................................................. viii

Acknowledgements .................................................................................................................... xi

1. Introduction ............................................................................................................................. 1

  1.1 Positron Emission Tomography .......................................................................................... 1

    1.1.1 Overview ....................................................................................................................... 1

    1.1.2 Reconstruction .............................................................................................................. 4

    1.1.3 Acquisition Modes ....................................................................................................... 5

    1.1.4 Image Quality ............................................................................................................ 7

      1.1.4.1 Spatial Resolution ................................................................................................. 7

      1.1.4.2 Attenuation Correction ......................................................................................... 7

      1.1.4.3 Random Events ..................................................................................................... 8

      1.1.4.4 Scatter Correction ............................................................................................... 8

      1.1.4.5 Noise ....................................................................................................................... 9

  1.2 Clinical Applications ........................................................................................................ 9

  1.3 Research Goal .................................................................................................................. 10

2. Methods and Materials ......................................................................................................... 12

  2.1 Patient Data ...................................................................................................................... 12

  2.2 Phantom Studies ............................................................................................................. 14

    2.2.1 Bladder Scatter Phantom .......................................................................................... 14

    2.2.2 Bladder Lesion Phantom ........................................................................................ 16
2.2.2.1 Background Activity ................................................................. 17
2.2.2.2 In Air .................................................................................... 18

3. Results and Discussion ......................................................................... 19
  3.1 Patient Data .................................................................................. 19
  3.2 Phantom Studies .......................................................................... 25
    3.2.1 Bladder Scatter Phantom Results ........................................... 25
    3.2.2 Bladder Scatter Phantom Discussion .................................... 30
    3.2.3 Bladder Lesion Phantom ....................................................... 36
      3.2.3.1 Background Activity Results ......................................... 37
      3.2.3.2 Background Activity Discussion .................................. 42
      3.2.3.3 In-Air Results ............................................................... 44
      3.2.3.4 In-Air Discussion .......................................................... 48
  4. Conclusions ..................................................................................... 49

Appendix A ........................................................................................... 50

References ............................................................................................ 52
List of Figures

Figure 1: Positron annihilation illustration ................................................................. 1

Figure 2: Illustration of a ring of detectors showing annihilation coincidence detection recording an annihilation event [courtesy of T.G. Turkington] ............................................. 2

Figure 3: From left to right: CT image showing anatomical detail. PET image showing biological uptake. PET/CT fusion image. (4) ......................................................................................... 3

Figure 4: Graphical depiction of 2D and 3D acquisition modes .......................................... 6

Figure 5: Torso phantom (left) top view and (right) side view. The torso phantom dimensions are 39x 36 x 21 cm (length x major axis x minor axis) .................................................. 14

Figure 6: Bladder lesion phantom insert (A) outside of the torso phantom with several surrounding lesions and (B) inside the torso phantom with the final nine lesions. (C) Full torso and bladder phantom setup. ........................................................................ 16

Figure 7: Histogram of bladder volumes of 67 patients ....................................................... 19

Figure 8: Histogram of bladder radioactivity levels of 67 patients......................................... 20

Figure 9: Histogram of bladder radioactivity concentrations of 67 patients ....................... 21

Figure 10: Histogram of background radioactivity concentrations of 67 patients .............. 21

Figure 11: Histogram of relative bladder to background uptake ratio of 67 patients .......... 22

Figure 12: Scatter plot of bladder volume versus total radioactivity of 67 patients .......... 23

Figure 13: Scatter plot of bladder volume versus radioactivity concentration of 67 patients ......................................................................................................................... 24

Figure 14: DSTE 2D acquisition of bladder scatter phantom showing four ROIs measured for all 47 slices with the bladder (A) in the center of the FOV, (B) on the edge of the FOV, and (C) outside of the FOV. ROI legend is shown in (A) only ......................... 26

Figure 15: Bladder scatter phantom data. DSTE 3D acquisition showing four ROIs measured for all 47 slices with the bladder (A) in the center of the FOV, (B) on the edge of the FOV, and (C) outside of the FOV. ROI legend is shown in (A) only ............ 28

Figure 16: Zero-bladder activity ROI measurements for 2D (top) and 3D (bottom) scans normalized to the mean of all ROIs. All within approximately 5% of a value of 1 showing inherent fluctuation. Notice buoyancy issue with top ROI interfering with air in bladder .................................................................................................................................. 29
Figure 17: Bladder scatter phantom image showing the location of four background ROIs. ROIs were applied to all slices within an image set.

Figure 18: 2D acquisition for (A) the center of FOV scan showing a large void ring surrounding the bladder (B) The edge of the FOV scan showing void ring artifact surrounding the bladder.

Figure 19: Example slice of the edge of FOV scan showing a void where the plastic cube is located.

Figure 20: 3D acquisition of (A) the center of FOV scan showing a most noticeable void directly above the bladder. (B) The edge of the FOV scan showing void artifact predominately on the left and right sides of the bladder.

Figure 21: Linear trend fitting to outside the FOV scan for an average of left and right side ROIs (top) and bottom ROI (bottom). Top ROI was not fitted due to ‘cube’ artifact. X refers to slice number following location of bladder and the intercept is a normalized concentration value.

Figure 22: Labeling schematic of nine lesions shown on cold bladder with background activity images.

Figure 23: Group 1 lesions shown for 2D (top) and 3D (bottom) acquisition with background radioactivity on the DSTE. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.

Figure 24: Group 1 lesions shown for 3D (top) and TOF (bottom) acquisition with background radioactivity on the D690. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.

Figure 25: Group 2 lesions shown for 2D (top) and 3D (bottom) acquisition with background radioactivity on the DSTE. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.

Figure 26: Group 2 lesions shown for 3D (top) and TOF (bottom) acquisition with background radioactivity on the D690. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.

Figure 27: DSTE 2D acquisition of the bladder lesion phantom with the mean activity level (left) and high activity level (right) showing void artifacts.
Figure 28: Radioactivity concentrations of Group 1 lesions shown for 2D (top) and 3D (bottom) acquisition in air on the DSTE ..........................................................44

Figure 29: Radioactivity concentrations of Group 1 lesions shown for 3D (top) and TOF (bottom) acquisition in air on the D690 ..............................................................................................................45

Figure 30: Radioactivity concentrations of Group 2 lesions shown for 2D (top) and 3D (bottom) acquisition in air on the DSTE ..............................................................................................................46

Figure 31: Radioactivity concentrations of Group 2 lesions shown for 3D (top) and TOF (bottom) acquisition in air on the D690 ..............................................................................................................47
Acknowledgements

I would first like to thank my advisor Timothy Turkington, Ph.D., for all his guidance throughout this process. A special thank you goes out to Joshua Wilson, Ph.D., and Robin Davis for their assistance in phantom filling and set-up.
1. Introduction

1.1 Positron Emission Tomography

Positron Emission Tomography (PET) is a functional imaging technique that uses positron emitting radiotracers to study biological processes within the human body.

1.1.1 Overview

A PET procedure introduces a radiotracer into the body that emits positrons as it decays. An emitted positron interacts with an electron through positron annihilation to produce an anti-parallel emission of two 511 keV photons. Using coincidence detection, PET utilizes this annihilation to non-invasively record the location of the radioactive elements (1).

![Positron annihilation illustration](image)

Figure 1: Positron annihilation illustration

PET scanners are composed of stationary rings of block detectors made from scintillation crystals coupled with photomultiplier tubes. An Annihilation Coincidence Detection (ACD) system records an event when two photons hit two detectors within a given time.
and energy window. The line on which an annihilation event occurs is called a line of response (LOR).

Clinical PET resulted from decades of development. It began with Ernest O. Lawrence’s invention of the cyclotron and identification of positron emitting nuclides in the 1930s. As technology advanced, cyclotrons became more efficient and accessible, making radionuclides readily available (2). In the 1950s, Benedict Cassen’s rectilinear scanner and Hal Anger’s gamma camera provided the first images of a distribution of radioactivity within the body (1). Gordon Brownell at MIT invented the first annihilation detection device that same decade, a precursor to the modern PET system. However, it was not until the filtered back projection reconstruction algorithm was developed for CT and applied to PET that the system came together (2). In 1974, Michael E. Phelps, Jerry Cox and Edward Hoffman had all the components to create the first PET scanner, called PET III. PET III was composed of a hexagonal arrangement of 48 NaI(Tl) detectors that used a 60 degree rotation of the gantry for sampling and coincidence detection (3). The
first human PET image was created in the 1970s, but several more decades would pass before it was clinically implemented for purposes other than research.

The determining factors of clinical PET were the development of $^{18}$F-FDG by two radiochemists, Al Wolf and Joanna Fowler in 1976, and the Medicare coverage for whole body PET imaging in treatment and diagnosis for cancer by 1999 (2). Only once PET was reimbursable was it able to transition to wide-spread clinical use. As a result of the work of David Townshend, the first integrated commercial PET/CT scanners became available in 2001, providing straight-forward attenuation correction as well as anatomical detail and fusion capabilities. All modern PET scanners now come as integrated PET/CT systems.

![Figure 3: From left to right: CT image showing anatomical detail. PET image showing biological uptake. PET/CT fusion image. (4)](image-url)
1.1.2 Reconstruction

Each LOR provides a sum of coincidence detections that is proportional to the amount of radioactivity along that line. The set of LORs for a given, fixed angle is known as a projection profile. For a single ring of detectors, a set of projection profiles covering 360 degrees of rotation can be acquired and represented in the form of a sinogram—a pictoral representation of the Radon transform (5). A sinogram represents a 2D cross-sectional slice within the body and can be reconstructed tomographically.

Backprojection is a common approach for image reconstruction, a concept that sums the projection profiles from each angle and projects them back across an image grid with finite pixels values. However, backprojection produces a representation of the object that is limited by a radial blurring effect (1/r). A method known as filtered backprojection (FBP) employs the use of a ramp filter (and other various filters) to eliminate this radial blurring effect. FBP is computationally simple and fast but is associated with high-frequency noise and edge sharpening artifacts (1).

Iterative reconstruction is prevalent among clinical PET applications. It differs from FBP by successively approximating the true image with a compute and compare algorithm. The algorithm begins with an estimate image and uses forward projection to bin intensities and calculate projections that would be measured from such an image. These calculations are represented in a sinogram that is compared to the actual recorded events sinogram. The difference between the computed image and true image is used to update the estimated image, until the estimated image converges to the true image. This process is computationally intensive and time consuming, partially because system
specific corrections are implemented such that each pixel must be considered rather than an entire path ray; the algorithm can incorporate corrections for blur, scatter and attenuation (1).

A popular iterative algorithm is Maximum-Likelihood Expectation-Maximization (MLEM). It predicts radioactivity distribution through weighting portions of the projection profiles; greater weight for the high count elements and less weight for the low count elements. In an attempt to reduce computation time to MLEM, an algorithm known as Ordered Subsets Expectation Maximization (OSEM) was introduced that divides the projections into subsets. The image can be updated and compared using one of these subsets of projection angles, known as a subiteration. A full iteration is a composition of $n$ subiterations, which is equal to defined number of subsets (6). Iterative reconstruction is more computationally intensive than FBP.

1.1.3 Acquisition Modes

Only 2D PET incorporates the use of septa between each ring of detectors. Septa, made from tungsten or lead, extend from the edges of the detectors to reject photons that are not parallel to the detector ring. Only lines of response within direct planes and cross planes (crystal rings directly adjacent to one another) are acquired in 2D PET, meaning a scanner with $n$ rings of crystals will produce an image set with $(2n - 1)$ axial planes. These 2D axial slices can be stacked to form a volumetric representation.
Acquisition in 3D mode removes the septa to allow lines of response from oblique planes. This greatly increases the sensitivity, but increases scatter and random events as well. Reconstruction is based on a 3D reconstruction algorithm that simultaneously reconstructs the entire image set rather than individual slices.

A more recent improvement to PET acquisition is known as Time-of-Flight (TOF) PET. This technique records the time difference between the two photons in a coincidence event to narrow down the annihilation location within a LOR. The location of the annihilation with respect to the center of the LOR can be calculated by

$$\Delta d = \frac{c\Delta t}{2}$$

where $\Delta d$ is the location, $c$ is the speed of light and $\Delta t$ is the recorded difference in time of the annihilation coincidence. The limiting factor of this improvement is the speed of the current available scintillators used in PET (1).
1.1.4 Image Quality

1.1.4.1 Spatial Resolution
Several factors limit the spatial resolution of a PET system including the positron range, non-collinearity and individual detector size. Before undergoing annihilation, an emitted positron can travel on the order of several mm depending on its energy and the density of the object (1). The ACD system identifies a LOR for which an annihilation event occurred, not where the positron was emitted, which results in a fundamental uncertainty in the radionuclide’s location. Non-collinearity refers to the fact that the annihilation photons are not emitted exactly 180 degrees apart due to residual momentum, an effect that causes resolution blurring. Finally the resolution is limited to the intrinsic spatial resolution of the detector elements. The system resolution of a PET scanner is a combination of these limiting factors.

1.1.4.2 Attenuation Correction
The majority of photons emitted do not reach the PET detectors due to Compton scattering in tissue. This process causes an underestimation of emitted photons, particularly in the center, and is dependent on patient size. To get an estimate of the attenuation correction, a CT image of the patient is acquired prior to the PET acquisition. Attenuation coefficients are energy dependent and must be corrected to values for 511 keV photons before applying to the PET data. An attenuation correction factor (ACF) is calculated for each sinogram element by integrating the attenuation coefficients with respect to distance $x$ along the LOR (7). The ACF can be represented in the following equation.
where $\mu (E, x)$ is the energy and distance dependent attenuation coefficient. Attenuation correction is the most significant correction that must be applied to PET images.

### 1.1.4.3 Random Events

The ACD system uses a timing window ($\tau$) of several nanoseconds (1) for which it considers a true coincidence event. A random event can be defined as two photons hitting two detectors that did not originate from the same emission, but occur within the ACD timing window. These “randoms” contribute background to the images and should be eliminated by one of two correction methods—the singles based method or delayed window method. The singles method is based on the individual detector rates ($R_1, R_2$) and is defined as

$$Randoms\ Rate = 2\tau R_1 R_2$$

The delayed window method directly calculates the random coincidence events by delaying the coincidence timing window an amount much larger than its acceptance width. Since one side of the coincidence unit is delayed, no true or scatter events will be recorded and an estimate of the random events rate is obtained. A real-time subtraction of this estimate from the total number of prompts corrects for random events (8).

### 1.1.4.4 Scatter Correction

Photons can undergo Compton scattering as they travel through matter. Due to the limited energy resolution of the PET detectors and because a number of the scattered photons do not lose enough energy, the energy discrimination window is not sufficient in complete scatter rejection (9). A scattered event occurs when an annihilation photon
scatters in matter and hits a detector other than the one on its original path. This results in a false LOR. A large fraction of scattered photons are eliminated in 2D PET by the presence of the septa, while the rest are typically corrected using a deconvolution method developed by Bergstrom, et al (10).

The typical scatter correction used in 3D PET is a single scatter simulation (SSS) algorithm, which estimates scatter contributions with emission and transmission images (11). The scatter probabilities are summed for each point in a transmission image and detector pair to estimate the distribution, and then scaled using a tail-fit method—a fit to match the tails of the measured data at each projection. The scattered event estimate is subtracted from the random-corrected prompts (11).

1.1.4.5 Noise

PET counts are subjected to Poisson probability law due to the statistical nature of radioactive decay (5). The random noise produces a “mottled” look within the images and it is important to obtain enough counts to ensure a good signal-to-noise ratio (SNR).

1.2 Clinical Applications

PET imaging is now widely accepted within the clinic and can be used as an oncology tool for initial patient staging and post-therapy response evaluation. The most common beta-emitting radionuclide used in PET imaging is $^{18}$F-2-Fluoro-2-deoxy-D-glucose (FDG), a glucose analog in which an OH is replaced with radioactive $^{18}$F. Malignant tumors tend to have a higher uptake of the glucose analog than healthy tissue due to an
increased rate of glycolysis (12). This allows assessment of glucose metabolism for clinical diagnosis of cancer, neurological disorders or myocardial diseases (1).

The voxels of a PET image are measures of radioactivity concentration within the body. An index commonly used in clinical practice is the Standardized Uptake Value (SUV), a normalized measure of radioactivity concentration (13). SUV is defined in the following equation

\[
SUV = \frac{\text{radioactivity concentration}}{\text{injected activity/patient mass}}
\]

where the radioactivity concentration is taken from a region-of-interest (ROI) on the PET image, i.e. a lesion or tissue.

SUV values are usually reported to be the maximum value of all voxels, \(SUV_{\text{max}}\), or the mean value over all voxels, \(SUV_{\text{mean}}\), within the defined ROI. While a decrease in SUV can be used as an indicator for therapy response, there is currently no established protocols (12). This is a consequence of SUV’s dependence on parameters outside of the user’s control including biological factors such as body size and blood glucose level, and inter-observer issues such as defining regions of interest and reconstruction methods (13).

1.3 Research Goal

There have been several studies showing positive results for \(^{18}\text{F}-\text{FDG PET/CT prediction of post-therapeutic tumor response in locally advanced rectal cancer}\) (14) (15) (16) (17), ovarian cancer (18) and uterine cancer (19). These studies use some variation of SUV as a predictor tool for pathological response to therapy, discrimination of responders from
non-responders and prediction of long-term outcome (14) (15) (16) (17) (18) (19). There is also evidence that the use of SUV$_{\text{mean}}$ measurements is reproducible in malignant tumors when taken several days apart (20).

A problem with this assessment involves the relative location of rectal carcinomas and gynecologic cancers in regards to the bladder. The bladder is constantly filling and an area of high activity in PET image. It has not yet been determined how this affects surrounding activity concentration values, and is difficult because bladders vary greatly from patient to patient. Because most $^{18}$F-FDG PET/CT predictor studies look towards quantification on a percentage or threshold basis, it would be appropriate to understand how much of the percentage change in an SUV could be associated with bladder activity. The purpose of this research is to assess the effects of bladder radioactivity on its surroundings.
2. Methods and Materials

2.1 Patient Data

An investigation of 67 Duke University Medical Center (DUMC) $^{18}$F FDG PET scans was performed using ROI analysis. The DUMC PET Facility performs PET/CT scans on two scanners; the GE Discovery STE (DSTE) and GE Discovery 690 (D690). The GE Discovery STE is a 24-ring bismuth germinate (BGO) PET system and 16 slice CT system. There are 560 BGO crystals per ring, each measuring 4.7 mm × 6.3 mm × 30 mm (tangential × axial × radial), and 23 retractable tungsten septa (21). The GE Discovery 690 system is a 24-ring Cerium-doped Lutetium Yttrium Orthosilicate (LYSO) PET system and 64 slice CT system. There are 13,824 LYSO crystals of size 4.7 x 6.3 x 25 mm$^3$ (tangential × axial × radial) (22).

Patients are restricted from eating for at least 4 hours prior to a scan but are encouraged to drink water (23). Blood glucose level is measured and may be no higher than 200mg/dL (23). Patients are intravenously injected with $^{18}$F FDG and required to rest for a minimum of one hour in a darkened room to allow proper uptake time, during which the patient is given an iodine-based oral contrast (23). Prior to being set-up on the scanner, patients are asked to void to reduce radioactivity within the bladder.

Patients are set up for the DUMC standard skull-base to mid-thigh (SBMT) scan, which translates the patient head first through the scanner bore, beginning acquisition at mid-thigh and ending at the skull-base (23). It purposely begins below the pelvic area to avoid as much bladder filling as possible. Once the set-up is complete, the technologist
performs a CT scout to confirm patient positioning. A full CT scan is then performed for attenuation correction purposes, followed by a 10-40 minute PET scan depending on patient size. For whole body PET imaging, after completion of the SBTM scan, the patient is taken off the scanner to be rotated and repositioned for a 10 minute leg scan. Patient images are reconstructed with all appropriate corrections for attenuation, scatter and random events. The images are reconstructed with a 50 cm FOV in a 128 x 128 matrix, resulting in individual voxels measuring 3.91 mm x 3.91 mm x 3.27 mm. Iterative reconstruction is used for the GE Discovery STE 2D and 3D mode, 2 iterations with 20 subsets, and the GE Discovery 690, 2 iterations with 24 subsets in non-TOF mode and 2 iterations with 16 subsets in TOF mode.

The ROI analysis explored parameters including bladder volume, radioactivity concentration within the bladder, total radioactivity within the bladder, radioactivity concentration of the background and bladder-to-background uptake ratio. The volumes of the patient bladders were measured by drawing an ROI to fully encompass the bladder and applying a threshold based on ¼ of the maximum pixel value. The volume was calculated by multiplying the total number of pixels within the thresholded ROI by the volume of an individual voxel. The radioactivity concentration within the bladder was determined to be the mean of a reduced bladder ROI focused on a more central region of the bladder to eliminate boundary fall-off effects. Total activity was calculated by multiplying the measured concentration with the calculated volume. A large ROI was drawn on the upper thigh of each patient, a combination of muscle and fat, to determine the mean radioactivity concentration of the background. Measurements of
relative bladder-to-background uptake ratio were performed by dividing each subject’s bladder concentration by that subject’s background concentration.

2.2 Phantom Studies

Measured parameters of the patient data study including bladder volume, radioactivity concentration within the bladder, total radioactivity within the bladder, radioactivity concentration of the background and bladder-to-background uptake ratio were used in the development of a bladder phantom insert.

2.2.1 Bladder Scatter Phantom

An oval ‘torso’ phantom, 39 cm x 36 cm x 21 cm (length x major axis x minor axis), was used to simulate the body for the various phantom studies.

Figure 5: Torso phantom (left) top view and (right) side view. The torso phantom dimensions are 39x 36 x 21 cm (length x major axis x minor axis)

An accessible insert was developed to model the bladder and investigate the position of an area of high activity in regards to the scanner FOV. The bladder insert is a sphere with two threaded holes on opposite sides that supported lure-lock inserts. The inserts
were connected to tubes that fed to the outside of the torso phantom and provided a pathway for injecting and removing radioactivity. The sphere was suspended from the top of the torso phantom to be vertically and horizontally centered.

The phantom was filled to a 46:1 bladder-to-background uptake ratio based on the results from 2.1. The phantom was scanned on the GE Discovery STE for four scenarios; a zero-activity bladder for normalization purposes (cold), and three hot bladder scans at the center of the FOV (center), the edge of the FOV (edge) and the outside the FOV (outside). Each scan was acquired in both 2D and 3D, for a total of eight scans. One bed position was acquired for 180 seconds per scan. The images were reconstructed with a 50 cm FOV for a 128×128 matrix, resulting in individual voxels measuring 3.91 mm x 3.91 mm x 3.27 mm, and appropriate corrections for attenuation, scatter and random events were applied. Iterative reconstruction was used with 2 iterations, 20 subsets for both 2D and 3D images.

ROI analysis was applied to four areas surrounding the bladder—the immediate left, right, top and bottom (shown in the Results section) of all 47 image slices to explore the effects of the bladder radioactivity on the surrounding background concentrations. The measured concentrations were corrected for decay and normalized to the background radioactivity concentration of the cold bladder scans. The normalization value was the average of the four background ROI concentrations.
2.2.2 Bladder Lesion Phantom

Figure 6: Bladder lesion phantom insert (A) outside of the torso phantom with several surrounding lesions and (B) inside the torso phantom with the final nine lesions. (C) Full torso and bladder phantom setup.

The bladder insert was also used to assess effects on surrounding lesions. An insert to hold the bladder and surrounding lesions was centered in the torso phantom. The bladder was centered on the insert, and nine 1-cm (0.5 ml) spheres were placed at varying distances from the bladder.
2.2.2.1 Background Activity

The torso phantom was filled to 1/8 its volume with room temperature water and background activity. Radioactivity levels included 0.46 mCi labeled ‘mean’ activity for the bladder, 0.9 mCi labeled ‘high’ activity for the bladder, and 1.68 mCi for the background activity (which was used for torso phantom and lesion filling) based on the results from 2.1. The 1-cm lesions were filled from this diluted activity to provide a 1:8 background to lesion radioactivity ratio. After all lesions were filled and secured, the remaining torso phantom was filled. The phantom was placed on the Discovery STE scanner for a total of six scans; three radioactivity levels with both 2D and 3D acquisition. The radioactivity levels included a cold bladder for normalization purposes (cold), a mean activity level (mean), and a high activity level (high). Once all eight scans on the DSTE were acquired, the phantom was relocated to the Discovery 690 where the process was repeated for both 3D and TOF acquisition.

The images were reconstructed with a 50 cm FOV for a 128x128 matrix, resulting in individual pixels measuring 3.91mm x 3.91 mm x 3.27 mm, and appropriate corrections for scatter and random events were applied. To explore lesion recovery based on image reconstruction, each acquisition was reconstructed with and without attenuation correction, as well as with protocol iterative reconstructions (2 iterations with 20 subsets in DSTE 2D/3D modes, and 2 iterations 24 subsets in D690 3D mode and 2 iterations with 16 subsets in TOF mode) and experimental iterative reconstructions that increased only the number of iterations to 5.
ROI analysis was applied to the 9 lesions for all image sets. The lesions were subdivided in two groups: the four closest distal lesions (1-4 cm) and five second closest distal lesions (> 4 cm). To simulate uptake ratio, the lesion concentration values were normalized to the background concentration of that particular image set. The background concentration values were determined by averaging large ROIs over several slices per image set. The concentration values were decay corrected prior to normalization.

2.2.2.2 In Air

To reduce scatter effects, the same acquisitions were performed with the bladder phantom with air instead of water with background radioactivity. The lesions were filled with the same radioactivity and volume of water as the background activity study. The bladder was scanned with three different activities on both PET/CT machines and the images were reconstructed as in 2.2.2.1. ROI analysis was applied in the same manner as 2.2.2.1 with the difference of normalization value. Since there was no background radioactivity to normalize to, the results are displayed with respect to radioactivity concentration.
3. Results and Discussion

3.1 Patient Data

Based on the mean volume of the patient sampling, a 100 ml sphere was chosen to model a bladder in the aforementioned phantom studies.

Modeling the total amount of activity within the bladder was not as straightforward, and required a more thorough investigation of the PET images. The patient distribution showed a mean of 0.158 mCi, but image artifacts were more apparent at higher radioactivity levels, and therefore more appropriate for further investigation. A versatile bladder phantom was developed to incorporate both the patient “worst case scenario” radioactivity (1.2-1.3 mCi) and above-average radioactivity (0.35-0.5 mCi), as seen in the

Figure 7: Histogram of bladder volumes of 67 patients

![Bladder Volume Histogram](image-url)
following figure. Actual radioactivity levels studied in the phantoms were 0.45 mCi and 0.9 mCi to achieve a 1:2 comparison.

![Graph](image-url)  

**Figure 8**: Histogram of bladder radioactivity levels of 67 patients

Two other parameters included radioactivity concentrations within the bladder and of the background. The patient study found a mean value of 2.8779 μCi/ml within the bladder and approximately 70 nCi/ml in the background. To achieve these concentrations, the calculated radioactivity for a 100 ml sphere is 0.3 mCi and for a 25 L torso phantom is approximately 1.75 mCi.
Figure 9: Histogram of bladder radioactivity concentrations of 67 patients

Figure 10: Histogram of background radioactivity concentrations of 67 patients
The significance of bladder-to-background uptake ratio as compared to exact radioactivity levels was also investigated. A measure of relative SUV was calculated for each patient. This value is an approximation and cannot accurately reflect the true uptake ratio because it is unknown how much of the activity was voided before the scan. The mean relative uptake ratio between the bladder and background tissue was approximately 45:1.

Figure 11: Histogram of relative bladder to background uptake ratio of 67 patients

mean = 45.0809
Scatter plots were used to establish any correlation between the bladder volume and total radioactivity, as well as the bladder volume and radioactivity concentration. The bladder is not a rigid structure, and varies greatly from patient to patient. Both scatter plots confirm the variable nature of radioactivity within the bladder. It can be seen from Figure 12 that the majority of bladders contained less than 0.2mCi in the volume range of 0-300 ml. However, there are two bladders less than 200 ml in volume that contain over 1 mCi of activity. This variability is further confirmed in Figure 13, where it is clear that a given bladder volume can have a large range of activity concentrations. Some of the largest volumes have low activity concentrations, which is to be expected.

![Volume vs Total Activity](image)

Figure 12: Scatter plot of bladder volume versus total radioactivity of 67 patients
Figure 13: Scatter plot of bladder volume versus radioactivity concentration of 67 patients
3.2 Phantom Studies

3.2.1 Bladder Scatter Phantom Results

Results are displayed in the following way: the y-axis represents a radioactivity concentration that has been normalized to the zero-activity bladder scan for its respective acquisition mode, 2D or 3D, i.e., a value of 1 correlates to concentration values that are unaffected by radioactivity within the bladder. The x-axis represents the image slice number. The ROI legend is only on the center scan graph.
Figure 14: DSTE 2D acquisition of bladder scatter phantom showing four ROIs measured for all 47 slices with the bladder (A) in the center of the FOV, (B) on the edge of the FOV, and (C) outside of the FOV. ROI legend is shown in (A) only.
Bladder in Center of the FOV: 3D

Bladder on Edge of the FOV: 3D
Figure 15: Bladder scatter phantom data. DSTE 3D acquisition showing four ROIs measured for all 47 slices with the bladder (A) in the center of the FOV, (B) on the edge of the FOV, and (C) outside of the FOV. ROI legend is shown in (A) only.
Figure 16: Zero-bladder activity ROI measurements for 2D (top) and 3D (bottom) scans normalized to the mean of all ROIs. All within approximately 5% of a value of 1 showing inherent fluctuation. Notice buoyancy issue with top ROI interfering with air in bladder.
3.2.2 Bladder Scatter Phantom Discussion

Recall that the four ROIs surround the bladder on the left, right, top and bottom, as shown in the following figure. The zero-activity scan had an air-filled bladder in the center of the FOV. The ROIs were drawn on a filled-bladder image set and applied later, so the top ROI was partially affected by a buoyancy issue, and is generally disregarded in the following results.

![Bladder scatter phantom image showing the location of four background ROIs. ROIs were applied to all slices within an image set.](image)

Figure 17: Bladder scatter phantom image showing the location of four background ROIs. ROIs were applied to all slices within an image set.

The 2D acquisition data shows consistent effects among all four background ROIs. In the 2D PET center scan, all four ROIs show a dramatic decrease, up to 25%, in radioactivity concentration within the axial slices containing the bladder, slices 17-35. This decrease can be attributed to a large void, ring artifact that surrounds the high activity bladder. Diversely, the background concentrations peak in the slices that immediately surround but do not directly contain the bladder.

The edge scan contains a version of the ring artifact that affects the left and right sides of an axial slice, up to 50%, more than the top and bottom, which is approximately 25%.
Again, the concentration values peak in the slices that immediately follow but do not directly contain the bladder (the bladder is located in slices 1-13). After peaking for several slices, the concentration values fall to the level of the normalization scan.

![Image](image)

**Figure 18:** 2D acquisition for (A) the center of FOV scan showing a large void ring surrounding the bladder (B) The edge of the FOV scan showing void ring artifact surrounding the bladder

In the outside scan, 2D PET shows radioactivity concentrations within 15% of the normalization scans in the majority of slices (with the exception of the top ROI in the first few slices which shows up to a 27% increase). This result is expected due to the effectiveness of the septa in initial scatter elimination in 2D PET.

It is seen that there is a noticeably smaller recovery of the top ROI in certain regions of slices for all bladder scatter data. The explanation for this is that the top ROI partially covers a region of no activity in certain slices—instead resides is a plastic cube that was used to stabilize the bladder’s position. This cube is not present in the center FOV scan, but does appear in slices 30-36 of the edge scan and 20-26 of the outside scan.
The 3D acquisition data shows several differences from the 2D acquisition data. In the center scan, there is an overall decrease in radioactivity concentrations for all four ROIs, that resides just below the normalization value. The ROI placed above the bladder seems most affected, up to 25%, particularly in the slices directly containing the bladder, which seems to be partially attributed to a slight void artifact as seen in the following figure, as well as the issue seen in the cold bladder scan. Axial slices 15 through 28 show the worst recovery for the top ROI, which can be attributed to a void artifact shown in the following figure.

The edge scan shows a void artifact that predominately affects the areas to the left and right of the bladder, resulting in a decrease of radioactivity concentration measurements up to 25%. Oppositely, the top and bottom ROIs see an increase in radioactivity concentration as high as 30%. The 2D data shows a decrease in activity concentrations for all four ROIs, but less so for the top and bottom where as the 3D data affects all four areas surrounding the bladder equally percentage-wise, but with two opposite effects.
Another difference in 3D acquisition is seen in the slices immediately surrounding but not directly containing the bladder, which tend to hover around the normalization value, showing good recovery of cold bladder background radioactivity concentrations.

![Figure 20: 3D acquisition of (left) the center of FOV scan (left) showing a most noticeable void directly above the bladder. The edge of the FOV scan (right) showing void artifact predominately on the left and right sides of the bladder.]

Recall that the SSS scatter correction uses emission and transmission data to estimate the scatter for each point in an image. Scatter events do come from outside the FOV and if the algorithm is unaware of the radioactivity within the bladder, it cannot accurately correct for this. The effects of this can be seen in the 3D PET outside scan, where the first slices of the image, located superiorly to the bladder, show background radioactivity concentration increases up to 50%. The radioactivity concentrations are grossly over-estimated for 30 slices until recovery of the normalization values set in. The ROIs, with the exception of the top ROI which is affected by the ‘cube’ artifact, show a linear trend over the thirty slices immediately following the bladder.
Figure 21: Linear trend fitting to outside the FOV scan for an average of left and right side ROIs (top) and bottom ROI (bottom). Top ROI was not fitted due to ‘cube’ artifact. X refers to slice number following location of bladder and the intercept is a normalized concentration value.
The bladder scatter phantom data shows both the weaknesses and strengths of 2D and 3D PET in terms of scatter correction. The Bergstrom, et al, deconvolution method struggles in both the center and edge scan, where the high activity greatly affects the surrounding concentration values, but performs well in the outside scan due to the septa’s effectiveness in initial scatter elimination. The benefits of 3D PET are shown in the center and edge scans where the radioactivity concentration values are relatively unaffected by the activity in the bladder. However, the 3D outside scan radioactivity concentrations are grossly overestimated. The 3D scatter algorithm depends on the transmission and emission scans to provide distribution estimates, and therefore cannot accurately correct for the unknown.
3.2.3 Bladder Lesion Phantom

The nine lesions were labeled accordingly: posterior-1 (P1), posterior-2 (P2), right-1 (R1), right-2 (R2), left-1(L1), left-2 (L2), right anterior-1(RA1), left-anterior-1(LA1), superior-1 (S1). All lesions did not reside on the same plane and therefore appear in different slices of the image sets. The analysis separates the lesions into two groups based on their distal location from the bladder. Environments with and without background activity were considered.

Figure 22: Labeling schematic of nine lesions shown on cold bladder with background activity images
3.2.3.1 Background Activity Results

Lesion recovery is defined to be in comparison with the lesion measurements of the zero-activity bladder scan. Results of ROI analysis are divided into two groups and displayed as such. Group 1 lesions are 2-4 cm distal from the bladder and include P1, P2, R1, L1, and S1. Group 2 lesions are greater than 4 cm distally from the bladder and include R2, L2, LA1 and RA1.

The results are displayed in the following way: the y-axis represents the radioactivity concentration ratio between the lesion and background of that particular image set. The x-axis represents data sets from three bladder radioactivity levels (cold, mean and high), each reconstructed with two iterations and five iterations. All image sets have been corrected for attenuation; the non-attenuation corrected images did not provide reasonable measurements of radioactivity concentrations and were not suitable for further analysis. The first two locations on the x-axis of each graph represent the cold bladder scan and provide a baseline for comparison to the mean and high levels of radioactivity within the bladder. All data for the Group 1 lesions are shown before Group 2. The percentage change of any particular lesion’s radioactivity concentration as compared to the cold bladder reconstructed with 2 iterations is supplied in Appendix A.
Figure 23: Group 1 lesions shown for 2D (top) and 3D (bottom) acquisition with background radioactivity on the DSTE. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.
Figure 24: Group 1 lesions shown for 3D (top) and TOF (bottom) acquisition with background radioactivity on the D690. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.
Figure 25: Group 2 lesions shown for 2D (top) and 3D (bottom) acquisition with background radioactivity on the DSTE. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.
Figure 26: Group 2 lesions shown for 3D (top) and TOF (bottom) acquisition with background radioactivity on the D690. Radioactivity concentration ratio is the lesion activity concentration compared to the background of that particular image reconstruction.
3.2.3.2 Background Activity Discussion

Only one lesion in Group 1 was unaffected by the bladder radioactivity in the DSTE 2D PET data. This lesion, S1, differs from the other lesions in that it is not located in any axial plane with the bladder. Rather, S1 is superior to the bladder. The other lesions show a lesion recovery less than one, meaning the ROIs contain less activity than the background. As seen in the bladder scatter phantom, this can be attributed to a void ring artifact. It is shown in the next figure that this artifact worsens as the radioactivity is increased, which is confirmed in the ROI analysis. Lesions are almost indistinguishable in this particular image set.

![Figure 27: DSTE 2D acquisition of the bladder lesion phantom with the mean activity level (left) and high activity level (right) showing void artifacts](image)

The DSTE 3D acquisition data does not show large void artifacts, making all Group 1 lesion recovery values greater than 1. For images reconstructed with two iterations, lesion recovery decreases as the activity in the bladder increases. The measurement
variability appears to double as the amount of radioactivity doubles. The data reconstructed with five iterations show better recovery, but increased variability, as expected due to the higher susceptibility to noise. However, lesion recoveries from reconstructions with 5 iterations are comparable to the cold bladder baseline measurements.

The 3D acquisition mode on the D690 shows an overall smaller Group 1 lesion recovery than 3D mode on the DSTE, particularly for the mean scan where most lesions are within 15% of their cold scan values. The concentration values are greatly affected by the high activity and are best when reconstructed with 5 iterations. Increasing the number of iterations for the mean activity only increased variability and shows no gain in recovery. The lesions on the right and left sides of the bladder show the smallest concentration values.

The TOF data shows the least amount of variability among Group 1 lesions for any particular data set. Again, the variability is lower in the images with 2 iterations, and increases in those with 5 iterations, and concentrations are higher in the reconstructions with 5 iterations.

Overall, the Group 2 lesions show much more consistent recovery than the Group 1 lesions. The 2D data shows a decrease in concentration with an increase in bladder activity. The 3D acquisitions on both the DSTE and D690 show very similar lesion recovery, with more variability on the DSTE. TOF acquisition results are very consistent and on a comparable scale to the cold bladder scan.
3.2.3.3 In-Air Results

To reduce scatter effects, the bladder lesion phantom was scanned in air. Results were not normalized as there was no background activity and do not represent relative uptake ratio. Results are displayed by radioactivity concentration measurements.

Figure 28: Radioactivity concentrations of Group 1 lesions shown for 2D (top) and 3D (bottom) acquisition in air on the DSTE.
Figure 29: Radioactivity concentrations of Group 1 lesions shown for 3D (top) and TOF (bottom) acquisition in air on the D690
Figure 30: Radioactivity concentrations of Group 2 lesions shown for 2D (top) and 3D (bottom) acquisition in air on the DSTE.
Figure 31: Radioactivity concentrations of Group 2 lesions shown for 3D (top) and TOF (bottom) acquisition in air on the D690
3.2.3.4 In-Air Discussion

There are many similarities between the background radioactivity and in air results.

Again, in 2D PET, only lesion S1 is unaffected by the bladder radioactivity while other Group 1 lesions showed greater decreases as radioactivity increased. This was expected due to the 2D PET’s presence of septa, which should eliminate a large portion of scatter regardless of scatter quantity.

The DSTE 3D data follows the same general pattern as the 2D data, but with overall higher radioactivity concentrations. Neither of the DSTE acquisitions resulted in Group 1 lesion concentration values equal to or exceeding the cold scan concentration values, even with 5 iterations.

The D690 acquisition data showed opposite results for the Group 1 lesions. Radioactivity concentration values rose almost 50% higher with radioactivity in the bladder than without. Furthermore, both the mean and high bladder resulted in the same lesion concentration measurements, and increasing the number of iterations did not substantially affect the variability. The TOF data follows suit, showing the same radioactivity concentration increases and variability among Group 1 lesions.

Group 2 lesions again show much more consistent recovery than the Group 1 lesions. Patterns of recovery reflect those lesions in Group 1, but with less variability among lesions of any one particular data set.

While the in air lesion phantom is a clinically unrealistic model, the data confirms that surrounding radioactivity measurements are affects by the presence of activity in the bladder.
4. Conclusions

It has been shown that radioactivity within the bladder has substantial effects on surrounding measurements. This data has justified the importance of patient voiding prior to PET/CT scanning, and validates the SBTM protocol at DUMC that begins acquisition below the pelvic area to reduce bladder filling. The following conclusions address the accuracy of the radioactivity concentration values used for SUV measurements in the vicinity of the bladder.

1. The 2D PET data suffers large void artifacts that worsen with increased radioactivity in the bladder. Radioactivity concentration measurements will not reflect true values.

2. The 3D PET data shows an over-estimation of background radioactivity concentrations in as many as thirty slices immediately following the location of bladder, if the transmission and emission data are unaware of bladder’s existence.

3. One should be cautious of SUV measurements for lesions less than or equal to 4 cm distal to the bladder. If measurements must be made, TOF acquisition shows the least amount of variability in radioactivity concentrations. If TOF capability is not an option, more iterations should be used in reconstruction for comparable radioactivity concentrations.

4. Lesions greater than 4 cm distal to the bladder show consistent recovery in both the 3D and TOF PET data.
Appendix A

Data from the bladder lesion phantom with background activity study. Percent change of any particular lesion’s radioactivity concentration as compared to the cold bladder scan reconstructed with 2 iterations concentration. Negative percent value represents a decrease in radioactivity concentration. Group 1 lesions denoted with a *

<table>
<thead>
<tr>
<th></th>
<th>DSTE 2D cold_5i</th>
<th>mean_2i</th>
<th>mean_5i</th>
<th>high_2i</th>
<th>high_5i</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1*</td>
<td>-0.20%</td>
<td>-60.14%</td>
<td>-48.72%</td>
<td>-95.39%</td>
<td>-96.56%</td>
</tr>
<tr>
<td>R1*</td>
<td>2.51%</td>
<td>-87.42%</td>
<td>-73.71%</td>
<td>-99.52%</td>
<td>-100.00%</td>
</tr>
<tr>
<td>P1*</td>
<td>-0.09%</td>
<td>-36.95%</td>
<td>-29.76%</td>
<td>-61.93%</td>
<td>-76.00%</td>
</tr>
<tr>
<td>S1*</td>
<td>-3.34%</td>
<td>10.30%</td>
<td>15.93%</td>
<td>3.78%</td>
<td>3.50%</td>
</tr>
<tr>
<td>L2</td>
<td>3.30%</td>
<td>-19.13%</td>
<td>-14.18%</td>
<td>-52.26%</td>
<td>-48.75%</td>
</tr>
<tr>
<td>R2</td>
<td>5.68%</td>
<td>-26.27%</td>
<td>-22.76%</td>
<td>-74.53%</td>
<td>-68.30%</td>
</tr>
<tr>
<td>LA1</td>
<td>2.38%</td>
<td>-28.40%</td>
<td>-25.06%</td>
<td>-41.10%</td>
<td>-37.20%</td>
</tr>
<tr>
<td>P2*</td>
<td>1.80%</td>
<td>-60.75%</td>
<td>-48.44%</td>
<td>-90.06%</td>
<td>-92.76%</td>
</tr>
<tr>
<td>RA1</td>
<td>3.32%</td>
<td>-42.34%</td>
<td>-40.15%</td>
<td>-65.05%</td>
<td>-61.43%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>DSTE 3D cold_5i</th>
<th>mean_2i</th>
<th>mean_5i</th>
<th>high_2i</th>
<th>high_5i</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1*</td>
<td>17.08%</td>
<td>-26.21%</td>
<td>-10.81%</td>
<td>-20.80%</td>
<td>9.58%</td>
</tr>
<tr>
<td>R1*</td>
<td>17.12%</td>
<td>-34.00%</td>
<td>1.47%</td>
<td>-47.00%</td>
<td>3.98%</td>
</tr>
<tr>
<td>P1*</td>
<td>23.45%</td>
<td>7.16%</td>
<td>36.26%</td>
<td>26.24%</td>
<td>40.95%</td>
</tr>
<tr>
<td>S1*</td>
<td>20.35%</td>
<td>-11.44%</td>
<td>5.64%</td>
<td>-38.68%</td>
<td>-25.90%</td>
</tr>
<tr>
<td>L2</td>
<td>11.32%</td>
<td>-16.79%</td>
<td>-5.66%</td>
<td>-13.55%</td>
<td>6.30%</td>
</tr>
<tr>
<td>R2</td>
<td>11.97%</td>
<td>0.59%</td>
<td>20.03%</td>
<td>-7.33%</td>
<td>16.50%</td>
</tr>
<tr>
<td>LA1</td>
<td>8.83%</td>
<td>-8.71%</td>
<td>-3.63%</td>
<td>5.79%</td>
<td>15.05%</td>
</tr>
<tr>
<td>P2*</td>
<td>14.85%</td>
<td>-27.19%</td>
<td>-8.64%</td>
<td>-32.57%</td>
<td>-15.44%</td>
</tr>
<tr>
<td>RA1</td>
<td>10.15%</td>
<td>-25.95%</td>
<td>-16.73%</td>
<td>-7.85%</td>
<td>13.62%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>D690 3D cold_5i</th>
<th>mean_2i</th>
<th>mean_5i</th>
<th>high_2i</th>
<th>high_5i</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1*</td>
<td>5.89%</td>
<td>7.07%</td>
<td>4.94%</td>
<td>-21.58%</td>
<td>-11.81%</td>
</tr>
<tr>
<td>R1*</td>
<td>6.98%</td>
<td>-15.00%</td>
<td>-23.25%</td>
<td>-53.08%</td>
<td>-23.92%</td>
</tr>
<tr>
<td>P1*</td>
<td>9.38%</td>
<td>-1.39%</td>
<td>45.77%</td>
<td>6.17%</td>
<td>12.41%</td>
</tr>
<tr>
<td>S1*</td>
<td>4.07%</td>
<td>-6.29%</td>
<td>-8.41%</td>
<td>-28.32%</td>
<td>-16.67%</td>
</tr>
<tr>
<td>L2</td>
<td>3.54%</td>
<td>-9.35%</td>
<td>-13.33%</td>
<td>-28.55%</td>
<td>-20.92%</td>
</tr>
<tr>
<td>R2</td>
<td>12.73%</td>
<td>-2.54%</td>
<td>-7.76%</td>
<td>-13.19%</td>
<td>-0.89%</td>
</tr>
<tr>
<td>LA1</td>
<td>4.57%</td>
<td>0.01%</td>
<td>-2.13%</td>
<td>-21.53%</td>
<td>-17.32%</td>
</tr>
<tr>
<td>P2*</td>
<td>2.28%</td>
<td>-2.85%</td>
<td>6.90%</td>
<td>-22.34%</td>
<td>2.18%</td>
</tr>
<tr>
<td>RA1</td>
<td>4.59%</td>
<td>0.37%</td>
<td>-7.46%</td>
<td>-30.35%</td>
<td>12.06%</td>
</tr>
<tr>
<td>D690 TOF</td>
<td>cold_5i</td>
<td>mean_2i</td>
<td>mean_5i</td>
<td>high_2i</td>
<td>high_5i</td>
</tr>
<tr>
<td>----------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>L1*</td>
<td>5.77%</td>
<td>-8.37%</td>
<td>12.01%</td>
<td>-13.83%</td>
<td>-8.01%</td>
</tr>
<tr>
<td>R1*</td>
<td>9.94%</td>
<td>-27.42%</td>
<td>-5.33%</td>
<td>-5.80%</td>
<td>10.46%</td>
</tr>
<tr>
<td>P1*</td>
<td>11.14%</td>
<td>-20.78%</td>
<td>8.40%</td>
<td>-27.01%</td>
<td>-16.22%</td>
</tr>
<tr>
<td>S1*</td>
<td>7.16%</td>
<td>-19.32%</td>
<td>-6.01%</td>
<td>-22.74%</td>
<td>-15.88%</td>
</tr>
<tr>
<td>L2</td>
<td>5.92%</td>
<td>-9.51%</td>
<td>-8.10%</td>
<td>-22.36%</td>
<td>-19.44%</td>
</tr>
<tr>
<td>R2</td>
<td>8.57%</td>
<td>-14.44%</td>
<td>-6.74%</td>
<td>-15.32%</td>
<td>-9.14%</td>
</tr>
<tr>
<td>LA1</td>
<td>2.50%</td>
<td>-11.36%</td>
<td>-7.95%</td>
<td>-23.07%</td>
<td>-21.96%</td>
</tr>
<tr>
<td>P2*</td>
<td>3.70%</td>
<td>-17.72%</td>
<td>-5.05%</td>
<td>-31.61%</td>
<td>-20.95%</td>
</tr>
<tr>
<td>RA1</td>
<td>8.28%</td>
<td>-12.03%</td>
<td>-4.59%</td>
<td>-20.71%</td>
<td>-16.57%</td>
</tr>
</tbody>
</table>
References


