QUANTITATIVE SPECT IMAGING OF PROSTATE CANCER

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JOHNS HOPKINS MEDICINE
SCHOOL OF MEDICINE
According to American Cancer Society estimates, ~180,400 men in the US were diagnosed with prostate cancer in 2000. Among them,

- ~11% are at high risk for metastatic spread of their disease
- ~30-40% of patients previously treated for prostate cancer developed symptoms of recurrent cancer that had not yet progressed to the point of skeletal involvement
ProstaScint® by Cytogen

- A diagnostic $^{111}$In labeled monoclonal antibody which specifically targets Prostate Specific Membrane Antigen (PSMA)

- Due to the selective expression of PSMA by prostate cancer cells, it can be used to detect the extent and spread of prostate cancer in the body
ProstaScint® by Cytogen

- $^{111}$In ProstaScint® is specifically approved by the FDA for use in two patient types:
  - newly diagnosed patients with biopsy-proven prostate cancer thought to be clinically localized after standard diagnostic evaluation and who are at high risk for spread of their disease to pelvic lymph nodes
  - post-prostatectomy patients in whom there is a high suspicion that the cancer has recurred
CATEGORIES OF MEDICAL IMAGING TECHNIQUES

Traditional (Planar Imaging)
- X-ray radiography
- Nuclear Medicine
- Ultrasound (US)

Modern (3D & 4D Imaging)
- X-ray computed tomography (CT)
- 3D ultrasound (US)
- Magnetic resonance imaging (MRI)
- Positron emission tomography (PET)
- Single-photon emission computed tomography (SPECT)

Emerging
- Electric Source Imaging
- Electrical Impedance Tomography
- Optical imaging
- Molecular imaging
CATEGORIES OF MEDICAL IMAGING TECHNIQUES

Anatomical
- X-ray radiography
- X-ray CT
- Ultrasound (US)
- Magnetic resonance imaging (MRI)

Functional
- Nuclear medicine
- Positron emission tomography (PET)
- Single-photon emission computed tomography (SPECT)
- Magnetic resonance imaging (MRI)
- Multi-Detector CT (MDCT)

Multimodality
- PET/CT, SPECT/CT
- MRI/PET, SPECT/CT/Optical
SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)

Combination of

2D Nuclear Medicine Imaging Techniques + Computed Tomography

Uses a variety of readily available radio-tracers in the nuclear medicine clinic
DIFFICULTIES IN IMAGING $^{111}$In PROSTASCINT®

- Biological distribution
- Limited amount of $^{111}$In that is allowable for injection due to radiation dose
- Low counts and very noisy data
- Physics in imaging $^{111}$In which emits 2 medium energy photons at 172 keV and 245 keV

Typical $^{111}$In ProstaScint® SPECT image obtained using 3D FBP algorithm without any correction and Processed using Butterworth, $n=8$, $fc=0.15/p$
ACHIEVING QUANTITATIVE $^{111}$In PROSTASCINT® SPECT

**Goals of Quantitative $^{111}$In ProstaScint® Imaging**
- improved image quality
- improved clinical diagnosis
- improved patient management

**Quantitation**
- Image degrading factors
- Compensation methods
- Image reconstruction methods

**Optimization**
- Instrumentation (collimator) design
  - Data acquisition methods
  - Image reconstruction methods

**Validation**
- Simulation studies
  - Computer generated phantoms
  - Monte Carlo methods
  - High speed computing
- Phantom studies
- Clinical studies
IMAGE DEGRADING FACTORS

**Instrumentation**
*collimator, detector*

**Patient Anatomy**
*attenuation distribution, body shape*

**Male – Flat Diaphragm**
**Male – Raised Diaphragm**
**Female – Large Breasts, Flat Diaphragm**

**Physical factors**
*attenuation, scatter, beam hardening*

**Patient Motion**
*respiratory motion, upward creep*
COMPENSATION OF FOR DEGRADING FACTORS FOR QUANTITATIVE ONCOLOGICAL SPECT IMAGING

Full 3D CDR function Compensation

Modeling complex 3D collimator-detector response

Attenuation Compensation
using attenuation map

Scatter Correction
using ‘effective scatter source’ method

Radionuclide TCT  X-ray TCT
MP SPECT uses $^{201}$Tl & $^{99m}$Tc that emit low-energy photons, i.e., $\sim 140$ keV

Oncology SPECT often involves radioisotopes that emit medium- and high-energy photons, e.g.,

<table>
<thead>
<tr>
<th>RADIONUCLIDE</th>
<th>PHOTON ENERGY (keV)</th>
<th>ABUNDANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ga-67</td>
<td>~83, ~93, ~185, ~300, ~393</td>
<td>~28%, ~37%, ~21%, ~17%, ~4.5%</td>
</tr>
<tr>
<td>I-131</td>
<td>~284, ~364, ~637</td>
<td>~6%, ~83%, ~7%</td>
</tr>
<tr>
<td>In-111</td>
<td>~144, ~172, ~247</td>
<td>~8%, ~91%, ~100%</td>
</tr>
</tbody>
</table>
QUANTITATIVE RECONSTRUCTION METHODS

Analytical FBP method without any compensation for image degrading factors

3D Iterative reconstruction methods with accurate 3D model of imaging process
COMMERCIAL TRANSMISSION CT SYSTEMS FOR ATTENUATION COMPENSATION

Scanning line source transmission CT systems

- SMV
- GE Optima
- ADAC Vantage

Transmission Imaging with Dual Scanning Gd-153 Line Sources

Stationary line source TCT systems

- Picker/Utah fan-beam stationary line source
- Picker Beacon™
- Siemens E.CAM™ with Profile™
- GE VG/Hawkeyes
Hybrid Imaging Process

**First Generation**
- Single slice & lower power CT
- Slower CT acquisition time
- Non-diagnostic quality CT images

**Second Generation**
- Multi-slice & higher power CT
- Faster CT acquisition time
- Diagnostic quality CT images
VALIDATION OF QUANTITATIVE SPECT METHOD

- Phantom studies
  - With known ‘truth’
  - Physical phantoms
  - Computer generated phantoms

- Projection data
  - Experimentally acquired data from physical phantoms
  - Monte Carlo simulated data from computer generated phantoms

- Quantitative image reconstruction methods
  - Conventional FBP algorithm without any correction
  - Iterative OS-EM with and without correction of degrading factors
  - New statistical image reconstruction algorithm with correction of degrading factors

- Patient studies
  - Patients with recurrent prostate cancer
3D NURBS-based Cardiac-Torso (NCAT) Phantom

Sample Slices from the Visible Human CT Data Set

NCAT Phantom (anterior view)

NCAT Phantom (posterior view)

3D NURBS Organ Models

Body  Skeleton  Lungs  Liver  Stomach  Spleen  Kidneys
Simulations Using the 3D NCAT Phantom

Emission Imaging

Myocardial SPECT Reconstructed Images

Transmission Imaging

X-ray CT Reconstructed Images
SIMULATION STUDY

Validation of Image Reconstruction Methods Using the Extended 4D NCAT Phantom

4D NCAT Phantom

Extended 4D NCAT Phantom

Left Lateral View of The Pelvic region
COMPUTER GENERATED DATA

• Goal
  – To accurately model data obtained from imaging equipment

• Requirements
  – Accurate modeling of
    • Photon emission from internal radioactive source distribution
    • Photon transport and interactions in patient
  – Photon transmission through collimator and interaction in crystal
    • collimator characteristics
      *i.e.*, *geometric, penetration and scatter components*
    • detector characteristics
      *i.e.*, *photon absorption and scatter in crystal*
MONTE CARLO SIMULATION METHODS

• Advantages
  – Can be used to accurately model the imaging process including instrumentation and physics

• Disadvantages
  – Very computationally extensive

• Available software packages
  – General purpose use
    • MCNP (Los Alamos National Lab)
    • EGS4 (http://www.slac.stanford.edu/egs/)
    • Géant4 (http://wwwinfo.cern.ch/asd/geant)
  – Special purpose use, e.g., for nuclear medicine imaging
    • SIMSET (University of Washington)
    • SIMIND (Michael Ljungberg, Lund University, Sweden)
    • GATE (OpenGATE consortium)
    • Others (e.g., U. of Chicago, Duke, MIT)
### ADVANCE IN COMPUTER HARDWARE

<table>
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</thead>
<tbody>
<tr>
<td>Typical Computer</td>
<td>DEC MicroVAX</td>
<td>DECstation 5000-200</td>
<td>DEC Alpha 3000-600</td>
<td>SUN Ultra 2</td>
<td>DEC PW 500 au</td>
</tr>
<tr>
<td>Computational Speed: SPECFP92 SPECFP95</td>
<td>3</td>
<td>20</td>
<td>160 5</td>
<td>500 11</td>
<td>20</td>
</tr>
</tbody>
</table>

### A Beowulf-Class Cluster (Since 1999)

*(Division of Medical Imaging Physics)*

- 64 rack mounted computers with dual processors ranging in speed from 800 MHz to 2.0 GHz
- Each has 15-80 GB disk and 256-512 MB (with 2 nodes having 2 GB) of memory
- The computers are connected by a 100 Mb or 1 GB Ethernet switch
- Linux operation system
Selected transaxial slices of the 3D NCAT phantom activity distribution modeling a typical uptake of $^{111}\text{In}$ ProstaScint® in a patient, showing the prostate in the leftmost slice, and with colored arrows pointing to several lymph nodes in the slides on the right.

The corresponding attenuation distribution of the selected transaxial slices from the 3D NCAT phantom shown above.
in the ascending portion of the large intestine

in the descending portion of the large intestine

in the rectum and lower portion of the sigmoidal colon
The data were over 360° around the 3D NCAT phantom. They were generated using the SimSET Monte Carlo simulation code. The data for the 172 KeV and 245 KeV photopeaks of $^{111}$In were generated separately, and then summed.
Filtered Backprojection algorithm (FBP) w/o any correction

A Butterworth postfilter with order 8

with attenuation correction (OSA)

with attenuation & detector response correction (OSAD)

~28,000 counts/slice

Iterative OS-EM algorithm (6 subsets)

~28,000 counts/slice

1st 3rd 5th 7th iterations.

0.10 0.12 0.14 0.16 cycles/pixel
In-111 ProstaScint® studies

Emission data acquisition
- IV administration of 5 mCi $^{111}$In ProstaScint®
- Siemens E.CAM dual-camera SPECT system with ME collimator
- 128x128 projection matrices
- 64 stops over 180° (128 views over 360°), 60 sec/view
- Non-circular orbit

CT data
- Transformed for use in attenuation compensation (AC)
- Fused with SPECT image

MRI data
- Segmented bone, soft tissue and air regions
- Assigned attenuation coefficients for use in AC
- Fused with SPECT image
PATIENT STUDY

71 yr old white male w/ post bilateral nerve sparing prostatectomy in 1996 & recent increased PSA

SPECT images show asymmetric radiotracer focus at the left common iliac vessel raises suspicion for lymph node involvement

UNC #12
Image slices #55 & #68, ~12,573 counts/slice
### In-111 PROSTASCINT® PROSTATE PATIENT STUDY

*(JHU #2/4D, GE VG/Hawkeyes SPECT/CT system)*

<table>
<thead>
<tr>
<th>Coronal CT image slices</th>
<th>SPECT coronal image slices (FBP)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1" alt="Coronal CT image slices" /> <img src="image2" alt="SPECT coronal image slices (FBP)" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SPECT coronal image slices (OS-EM)</th>
<th>Fused coronal SPECT/CT image slices</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="SPECT coronal image slices (OS-EM)" /></td>
<td><img src="image4" alt="Fused coronal SPECT/CT image slices" /></td>
</tr>
</tbody>
</table>
### PATIENT STUDY (#12)

<table>
<thead>
<tr>
<th>Cutoff Frequency (cycle/pixel)</th>
<th>Iteration Number</th>
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</thead>
<tbody>
<tr>
<td>0.10</td>
<td>1</td>
</tr>
<tr>
<td>0.15</td>
<td>2</td>
</tr>
<tr>
<td>0.20</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Method</th>
<th>Images</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D FBP w/o correction Butterworth, n=8</td>
<td><img src="#" alt="Image 1" /></td>
</tr>
<tr>
<td>OS-EM w/ CDR correction</td>
<td><img src="#" alt="Image 2" /></td>
</tr>
<tr>
<td>OS-EM w/ CDR, attenuation correction</td>
<td><img src="#" alt="Image 3" /></td>
</tr>
<tr>
<td>OS-EM w/ CDR, attenuation &amp; scatter correction</td>
<td><img src="#" alt="Image 4" /></td>
</tr>
</tbody>
</table>

**Potential image artifact:** breaking up of anatomical structure

Slice #76 ~12,573 counts/slice
STATISTICAL IMAGE RECONSTRUCTION ALGORITHMS

- OS-EM
  *(Ordered-Subset Expectation-Maximum) algorithm*

- Modified RBI-EM
  *(Relaxed-Block-Iterative Expectation-Maximum) algorithm*

- RAMLA
  *(Row-Action Maximum-Likelihood Algorithm)*

- RBI-MAP-EM
  *(Relaxed-Block-Iterative Maximum-A-Priori Expectation-Maximum) algorithm*
**Method – 4D MAP-RBI-EM**

### MAP-RBI-EM

- Developed based on ML-EM, RBI-EM, and MAP-EM-OSL
- Seeks the maximum *a posteriori* (MAP) solution given the measured projection data using prior information, and the fast rescale-block-iterative (RBI)\(^1\) expectation-maximization (EM) algorithm

\[
x_{i,t}^{\text{new}} = x_{i,t}^{\text{old}} + t_n^{-1} \left[ \sum_j c_{ij} x_{i,t}^{\text{old}} + \frac{\partial U(x)}{\partial x_{i,t}^{\text{old}}} \right]
\]

where

- \(x_{i,t}^{\text{old}}\): reconstructed image estimate at voxel \(i\) in time \(t\)
- \(p_{j,t}\): measured projection data at bin \(j\) in time \(t\)
- \(c_{ij}\): transition matrix which is used to model compensations
- \(S_n\): subset of the projection data
- \(U\): total energy
- \(t\): step size

Method – Gibbs Priors

Generalized Gibbs Prior

- Relationship between a pixel and its neighboring pixels

\[ P(x) = Z^{-1} e^{-\beta U(x)} \quad U(x) = \sum_{i,k \in NH} w_{ik} V_{ik} (x_i - x_k) \]

- where
  
  \( Z \): normalizing constant  \( w \): weight factor
  
  \( U \): total energy of image  \( V \): potential function
  
  \( \beta \): weighting parameter  \( NH \): neighborhood

4D Space-Time Gibbs Prior

- Prior for 4D MAP-RBI-EM
- Relationships among neighboring space-time voxels
- Smoothing in time dimension as well as spatial dimension

\[ \frac{\partial U(x)}{\partial x_{i,t}} = \beta_{\text{space}} \sum_{i,k \in NH} w_{ik} \frac{\partial V_{\text{space}}(x_{i,t} - x_{k,t})}{\partial x_{i,t}} + \beta_{\text{time}} \sum_{(i,t)(k,t+1) \in NH} w_{(i,t)(k,t+1)} \frac{\partial V_{\text{time}}(x_{i,t} - x_{k,t+1})}{\partial x_{i,t}} \]
**Method – The Derivative of a GPF**

The Derivative of a Generalized Potential Function (GPF)

- Ability to approximate any specific smoothing effect by choosing set of values of $\alpha$, $\delta$, and $\gamma$.

\[
\frac{\partial V(r)}{\partial r} = \frac{\gamma}{|r|} \left(1 - \frac{r}{2}\right) \left[1 + \alpha^2 \left(\frac{\delta}{r} - \frac{\delta}{\delta}\right)^2\right]^{\frac{1}{2}} + \gamma \left(\frac{r/\delta}{1 + |r/\delta|}\right) \propto \text{Smoothing Force}
\]

- $\delta$: position of the peak (target of smoothing)
- $1/\alpha$: width of the peak (range of smoothing)
- $\gamma$: height of the peak tail (convergence rate)
Comparing OS-EM and RBI-MAP-EM

Parameters:
- MAP A: $\alpha=0.3$, $\beta=0.02$, $\gamma=0.01$, $\delta=3$
- MAP A: $\alpha=0.3$, $\beta=0.02$, $\gamma=0.2$, $\delta=2$
- MAP A: $\alpha=0.3$, $\beta=0.03$, $\gamma=0.2$, $\delta=2$
PATIENT STUDY

SPECT images

JHU #P025

OS-EM with AC
32 updates
Post-filtered
clinical processing
PATIENT STUDY
SPECT images

JHU #P025

OS-EM with AC, CDRC & SC
12 updates
Post-filtered
PATIENT STUDY
SPECT images

JHU #P025

RBI-MAP-EM with AC, CDRC & SC
20 updates
No post-filtering
PATIENT STUDY

(Sample CT & SPECT images)

JHU #P025

OS-EM w/ AC only
32 updates
Post-filtered
clinical processing

OS-EM w/ AC, CDRC, SC
12 updates,
Post-filtered

RBI-MAP-EM w/ AC, CDRC, SC
20 updates, no filter
PATIENT STUDY (Fuses CT & SPECT images)

JHU #P025

OS-EM w/ AC only
32 updates
Post-filtered
clinical processing

OS-EM w/ AC, CDRC & SC
12 updates,
Post-filtered

RBI-MAP-EM w/ AC, CDRC, SC
20 updates, no filter
FUTURE STUDIES

- Optimization of quantitative $^{111}$In ProstaScint® SPECT image reconstruction methods
  - Simulated phantom data with known abnormal uptakes in prostate and lymph nodes
  - Lesion detection task
  - Computer and human observer studies

- Patient evaluation study
  - Patient recruitment
  - Comparing different image reconstruction methods for maximum clinical diagnosis
CONCLUSIONS

- Prostate SPECT imaging using $^{111}$In ProstaScint® requires the use of medium-energy collimators to image the 172 and 245 keV photons.
- The geometric, penetration and scatter components of the collimator-detector response (CDR) degrade reconstructed images quality.
- Careful modeling and implement of the CDR provide significant improvements in image quality.
- Additional attenuation and scatter compensation further improve image quality.
CONCLUSIONS

- Due to low detected counts, an observed artifact in the processed image is the breaking up of anatomical structures.
- New statistical image reconstruction methods to reduce the image artifacts are being investigated.
- Results from phantom and patient studies demonstrate the effectiveness of the quantitative SPECT image reconstruction methods.
- Validation and clinical evaluation of improved $^{111}$In ProstaScint® images are underway.
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THE END

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