Acquiring 4D CT data for Monte Carlo calculations

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Potential conflicts-of-interest

- I am PI of a sponsored research agreement between Stanford and Varian Medical Systems
Educational objectives

- Understand the mechanism and application of 4D CT imaging
- Understand the central role of deformable image registration in 4D dose calculations
- Understand a framework for 4D dose calculation
Introduction

- Accuracy of MC is limited by:
  - Input radiation source description
  - Accuracy of input geometry and materials
  - Physical processes modeled
  - Cross-sections

- This talk focuses on the patient geometric input, particularly the acquisition and use of time dependent CT images
Introduction

- Formalism developed for intrafraction respiratory motion but can be extended for interfraction adaptive radiotherapy
- Use of MC for 4D anatomic calculations is relatively new, however likely to increase in importance
  - 4D data more available
  - MC more available
  - Deformable image registration algorithms more available
  - Adaptive radiotherapy schemes becoming more available
- Overall desire to estimate the radiation dose as accurately as possible
Input requirements for 4D MC calculations

- 4D CT-capable scanner to create anatomic input
- Deformable image registration algorithm
- 4D-capable treatment planning system
- Commissioned Monte Carlo system
4D Monte Carlo flowchart

1. Create deformation fields from 4DCT
2. Define anatomy on reference CT
3. Map anatomy to all CT sets
4. Create Monte Carlo treatment plan on reference CT
5. Create treatment plan on all CT sets
6. Combine dose distributions and display on reference CT
4D CT Imaging
4D thoracic CT imaging

CT Controller

Images
Respiration Signal
X-Ray On Signal

CT Image Sorting Program

Peak Exhale
Mid Inhaler
Peak Inhaler
Mid Exhale

Vedam et al PMB 2003
What use are 4D CT scans?

- Determine tumor motion/screening
- Motion inclusive treatment
- Respiratory gated treatment
- 4D radiotherapy
4D CT imaging can be

- Ciné or helical acquisition
- Sinogram or image sorting
- Input signal can come from many sources
- Patient is limiting factor!
## Brief history of 4D thoracic CT

<table>
<thead>
<tr>
<th>Development</th>
<th>Year</th>
<th>First Author</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single slice helical</td>
<td>2003</td>
<td>Ford, Vedam</td>
<td>MSKCC, VCU</td>
</tr>
<tr>
<td>Multislice cine (commercial)</td>
<td>2003</td>
<td>Pan (2004)</td>
<td>GE/MGH/MSKCC</td>
</tr>
<tr>
<td>Cone beam (benchtop)</td>
<td>2003</td>
<td>Taguchi</td>
<td>Toshiba</td>
</tr>
<tr>
<td>Multislice cine</td>
<td>2003</td>
<td>Low</td>
<td>Washington University</td>
</tr>
<tr>
<td>Multislice helical</td>
<td>2004b</td>
<td>Keall</td>
<td>VCU, MDACC</td>
</tr>
<tr>
<td>Multislice cine PET/CT</td>
<td>2004a,b</td>
<td>Nehmeh</td>
<td>MSKCC</td>
</tr>
<tr>
<td>Cone beam (clinical)</td>
<td>2005</td>
<td>Sonke</td>
<td>NKI</td>
</tr>
<tr>
<td>Applications outside radiation oncology</td>
<td>2005-present</td>
<td>Guerrero, Keall¹, Low</td>
<td>MDACC, VCU, Washington University</td>
</tr>
</tbody>
</table>
8 respiratory phases
- Peak inhale
- Early inhale
- Mid inhale
- End inhale
- Peak exhale
- Early exhale
- Mid exhale
- Late exhale

Vedam et al PMB 2003 48:45-62

4D CT images
Respiratory variability

3 minutes later ...

Courtesy Sonja Dieterich, Georgetown University
### What 4D MD CT is available?

<table>
<thead>
<tr>
<th>Vendor</th>
<th>Respiratory signal</th>
<th>Ciné/Helical</th>
<th>Reconstruction Options</th>
<th>When Available?</th>
</tr>
</thead>
<tbody>
<tr>
<td>GE</td>
<td>Varian RPM Optical</td>
<td>Ciné</td>
<td>Image sorting based on displacement or phase of signal</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Philips</td>
<td>Varian RPM Optical + Bellows</td>
<td>Helical</td>
<td>Sinogram sorting based on respiratory “tags”</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Siemens</td>
<td>Abdominal belt</td>
<td>Helical</td>
<td>Sinogram sorting based on respiratory waveform</td>
<td>FDA approved</td>
</tr>
<tr>
<td>Toshiba</td>
<td>Abdominal belt</td>
<td>Ciné</td>
<td>Image sorting based on respiratory waveform</td>
<td>Spring 2006 (256 row)</td>
</tr>
</tbody>
</table>
Deformable image registration
Deformable image registration

- Non-rigid registration algorithms
- Map objects/pixels in one image to another
- Create a displacement vector field (DVF)
- Characterized by similarity metric and interpolation method
Deformable image registration

Source image

Target image

DVF (2D view)

DVF (3D view)
## Similarity metric and interpolation methods

<table>
<thead>
<tr>
<th>Similarity Metric</th>
<th>Interpolation Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutual information</td>
<td>Viscous fluid velocity field</td>
</tr>
<tr>
<td>Cross correlation</td>
<td>Optical flow</td>
</tr>
<tr>
<td>Minimum mean squared difference</td>
<td>Thin plate spline</td>
</tr>
<tr>
<td>Contour matching</td>
<td>B-spline</td>
</tr>
<tr>
<td></td>
<td>Finite element analysis</td>
</tr>
</tbody>
</table>
Finite element analysis

The fundamental equation of finite element analysis (FEA) for an elastic body is given by Hooke’s Law, shown in Equation (6),

\[ Ku = -F, \]  

where \( K \) is the stiffness matrix of the elastic material, \( u \) is the displacement vector, and \( F \) is the applied force. Equation (6) is solved by specifying boundary conditions, defined through forces or set displacements on a subset of the nodes in the finite element model. A finite element model is a series of connected points, or nodes, that when combined together to form a mesh, describe a volume of interest. The imple-
et al. 2005). The viscous-fluid, ordinary differential equation is given by Equation (7),

$$\frac{du(x, \theta)}{d\theta} = v(u(x, \theta), \theta),$$  

(7)

where $v(u, \theta)$ is the velocity field. The deformation field is solved by maximizing a similarity metric while constraining the deformation field to comply with the laws of continuum mechanics, resulting from viscous-fluid modeling using the Navier–Stokes equations on the velocity fields.
Optical flow is described by Equation (8),

$$\mathbf{u} = \frac{[I(x, \theta_k) - I(x, \theta_0)]\nabla I(\theta_0)}{[\nabla I(\theta_0)]^2 + [I(x, \theta_k) - I(x, \theta_0)]^2},$$

(8)

and $\mathbf{u} = (u_x, u_y, u_z)$, $\nabla I(\theta_0)$ is the gradient of the static image. The difference in the image intensity in the two images and the gradient of the static image, external and internal forces, respectively, act as competing forces, since the algorithm is optimized to minimize both. This algorithm was implemented by Thirion in the “demons” algorithm through an iterative process of solving Equation (8) and regularizing the deformation field using a Gaussian filter to smooth the deformation field (Thirion 1998). Wang et al. (2005a,b) have recently added active forces, based on the gradient of the moving image, to the demons algorithm to improve efficiency of registration, resulting in Equation (9).

$$\mathbf{u} = \left( I(x, \theta_k) - I(x, \theta_0) \right) \times \left( \frac{\nabla I(\theta_0)}{[\nabla I(\theta_0)]^2 + [I(x, \theta_0) - I(x, \theta_k)]^2} + \frac{\nabla I(\theta_k)}{[\nabla I(\theta_k)]^2 + [I(x, \theta_0) - I(x, \theta_k)]^2} \right)$$

(9)
Spline interpolation techniques use a grid of control points, or “knots,” to deform the image. The use of thin plate splines (TPS) was introduced by Bookstein (1989) to model biological shape changes such as deformation. The more knots, the more degrees of freedom the registration has, and each knot has a global effect on the entire image. TPS is based on the fundamental solution to the biharmonic equation,

\[ f(x, y, z) = |r|, \tag{10} \]

where \( r = \sqrt{x^2 + y^2 + z^2} \).

Hierarchical B-splines, which were first described by Forsey and Bartels (1988), consist of piecewise polynomial basis functions that affect only a local area of the image. A tricubic B-spline is defined in Equation (11), where \( b_{ijk} \) are the cubic B-spline basis functions and \( N_{ik} \) are the control points or knots in the volume.

\[ f(x, y, z) = \sum_{i=0}^{r} \sum_{j=0}^{s} \sum_{k=0}^{t} b_{ijk} N_{i}^{3}(x) N_{j}^{3}(y) N_{k}^{3}(z) \tag{11} \]

The bending energy, which is independent of any affine transformation that the source dataset undergoes, describes the amount of deformation that occurs between two states. Minimization of the bending energy of the perturbation is often used in TPS and B-spline implementation to avoid unrealistic deformations. The bending energy, a positive and unitless number, is defined in Equation (12).

\[ I[f(x, y, z)] = \iint \left( \left( \frac{\partial^2 f}{\partial x^2} \right)^2 + \left( \frac{\partial^2 f}{\partial y^2} \right)^2 + \left( \frac{\partial^2 f}{\partial z^2} \right)^2 + \left( \frac{\partial^2 f}{\partial xy} \right)^2 + \left( \frac{\partial^2 f}{\partial xz} \right)^2 + \left( \frac{\partial^2 f}{\partial yz} \right)^2 \right) dxdydz \tag{12} \]
Calculus of variations

similarity measure and the smoothness constraints applied. The voxels are allowed to move freely and are constrained through the minimization of the energy functional defined in Equation (13),

\[ \hat{u} = \arg \min \epsilon(u), \]  

(13)

where

\[ \epsilon(u) = \int_{x \in R^3} \left[ R^2(x, u) + \lambda \sum_{i=1}^{3} \sum_{j=1}^{3} (v^i_j)^2 \right] dx \]  

and

\[ v^i_j = \frac{\partial u^i}{\partial x^j}. \]  

(14)

The deformation field is then calculated by solving the Euler–Lagrange equation, Equation (15), using a finite difference method and a multi-resolution strategy.

\[ \lambda \nabla^2 u - R(x, u) \frac{\partial R(x, u)}{\partial u} = 0 \]  

(15)
**Accuracy**

- All DIR algorithms have uncertainties
- Very difficult to quantify on population or individual basis
- Error $O(\text{mm})$ that should not be ignored

<table>
<thead>
<tr>
<th>First Author</th>
<th>Similarity Metric</th>
<th>Interpolation Scheme</th>
<th>Anatomical Site</th>
<th>Accuracy Metric</th>
<th>Accuracy Average (sd) mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bharatha et al. (2001)</td>
<td>Contour, surface matching</td>
<td>FEA</td>
<td>Prostate</td>
<td>2 landmarks</td>
<td>1.01, 0.73 (0.56, 0.40)</td>
</tr>
<tr>
<td>Brock et al. (2003a)</td>
<td>MI</td>
<td>TPS</td>
<td>Liver</td>
<td>Bifurcations</td>
<td>LR: 1.3 (1.0) AP: 1.5 (1.2) SI: 1.5 (1.4)</td>
</tr>
<tr>
<td>Brock et al. (2005)</td>
<td>Contour, guided surface projection</td>
<td>FEA</td>
<td>Liver</td>
<td>Bifurcations</td>
<td>LR: 0.0 (1.4) AP: -1.0 (2.0) SI: 0.2 (1.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lung</td>
<td></td>
<td>LR: 1.3 (2.2) AP: 3.2 (2.3) SI: 0.5 (2.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breast/ Stomach/ Kidneys</td>
<td>Contours</td>
<td>LR: 0.3 (1.4) AP: 0.0 (1.6) SI: -0.3 (1.2)</td>
</tr>
<tr>
<td>Coelho et al. 2004</td>
<td>MI</td>
<td>TPS</td>
<td>Lung</td>
<td>Bifurcations</td>
<td>LR: 0.0 (1.7) AP: -0.5 (3.1) SI: 0.4 (3.6)</td>
</tr>
<tr>
<td>Keall et al. 2005</td>
<td>Min mean sq error</td>
<td>Viscous fluid</td>
<td>Lung</td>
<td>Bifurcations</td>
<td>&lt;4.0</td>
</tr>
<tr>
<td>Lu et al. 2004</td>
<td>E minimization Smoothness function of intensity difference</td>
<td>Lung</td>
<td>Prostate</td>
<td>Balloon phantom Image overlay CC</td>
<td>&lt;1 mm Qualitative CC: 0.98 – 0.99</td>
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<tr>
<td>Rietzel et al. 2005</td>
<td>Sum sq diff</td>
<td>B-spline</td>
<td>Lung</td>
<td>Difference images</td>
<td>Qualitative</td>
</tr>
<tr>
<td>Rohlfing et al. 2004</td>
<td>MI</td>
<td>B-spline</td>
<td>Liver</td>
<td>Surface Landmarks</td>
<td>4.0 2.7</td>
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<tr>
<td>Schaly et al. 2005</td>
<td>Contour</td>
<td>TPS</td>
<td>Prostate</td>
<td>Markers</td>
<td>3.0 (1.9)</td>
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<tr>
<td>Venugopal et al. 2005</td>
<td>Contour</td>
<td>TPS</td>
<td>Prostate</td>
<td>Volume overlap</td>
<td>97%</td>
</tr>
<tr>
<td>Wang et al. 2005b</td>
<td>CC or MI + active force</td>
<td>Optical flow</td>
<td>Prostate</td>
<td>Sim. defm Defm. phantom</td>
<td>0.5 (1.5) 0.8 (0.5)</td>
</tr>
<tr>
<td>Zhang et al. 2004</td>
<td>Contour, E minimization</td>
<td>FEA</td>
<td>Lung</td>
<td>Image overlay</td>
<td>Qualitative</td>
</tr>
</tbody>
</table>
4D dose computation framework
General framework: 3D and 4D

In 3-D radiotherapy planning, the estimated prescribed dose, $D_{Rx}$, is that computed on the anatomic space $x$ given the anatomy $I(x)$ and beam fluence $\Psi$,

$$D_{Rx} = D_{Rx} \left( x \mid \Psi, I(x) \right).$$  \hspace{1cm} (16)

When accounting for intrafraction changes over time $t$, the estimated prescribed dose is computed on a changing anatomy, $I(x,t)$. The beam fluence $\Psi(t)$ will in general be time dependent. In order to correctly integrate the dose for a given voxel, the time-dependent displacement vector field (DVF) from the DIR algorithm is also needed. Thus, the 4-D estimated prescribed dose is:

$$D_{Rx} \int_{\text{Image start}}^{\text{Image end}} d_{Rx} \left[ x + u(x,t) \mid \Psi(t), I(x,t) \right] dt,$$  \hspace{1cm} (17)
However, since the 4-D CT is discrete rather than continuous in time, Equation (17) is approximated by

$$D_{Rx} = \sum_{\text{Phase } k=1}^{p} \lambda_{Rx}^k d_{Rx} \left[ x + u(x, \theta_k) \right| \Psi_k, I(x, \theta_k) \right], \quad (18)$$

where $\lambda_{Rx}^k$ is a weight term accounting for variations in time spent in each discrete part of the respiratory cycle. The implications of this approximation are discussed in
General framework: 4D delivery

During treatment delivery, the respiratory signal and anatomy (and also potentially beam fluence) will vary from that planned, and thus the delivered dose $D_{Tx}^i$ for a given fraction is:

$$D_{Tx}^i = \sum_{\text{Phase } k=1}^{p} \lambda_{Tx}^k d_{Rx} \left[ x + u(x,\theta_k) \right] \Psi_{i,k}, I(x,\theta_{i,k}) .$$ (19)

Note that $\lambda_{Tx}^k$ will in general be different from $\lambda_{Rx}^k$, the time spent in respiratory phases during each radiation fraction. The delivered 4-D dose, summed over each $i$ of $N$ fractions, is given by:

$$D_{Tx} = \sum_{\text{Fraction } i=1}^{N} \sum_{\text{Phase } k=1}^{p} \lambda_{Tx}^{i,k} d_{Rx}^{i,k} \left[ x + u(x,\theta_{k})_i \right] \Psi_{i,k}, I(x,\theta_{i,k}) .$$
A clinically implemented treatment scenario (Shih et al. 2004; Starkschall et al. 2004) is to use 4-D CT for tumor spatial and temporal localization and to create a treatment plan that includes the observed tumor motion, as well as other errors such as expected variations in tumor motion, size and shape during therapy, and setup error (ICRU 1999). However there is no respiratory motion management during treatment delivery. In this case, the fluence is independent of treatment fraction and respiratory phase (i.e., $\Psi(t) \rightarrow \Psi$) and, thus, Equation (17) becomes:

$$D_{Rx} = \sum_{\text{Phase } k=1}^{p} \lambda_{Rx}^k d_{Rx} \left[ x + u(x, \theta_k) | \Psi, I(x, \theta_k) \right].$$  \hspace{1cm} (21)

Given the limitation of current planning systems, Equation (21), in the current planning of these treatments, the dose calculation is generally computed on a single CT image set without deformable image registration.
Motion inclusive treatment
Respiratory gating involves the temporal synchronization of the radiation beam-on/off signal with a respiratory signal. Beam-on only occurs for a certain number of respiratory cycle parts. Also, the beam fluence typically is independent of respiratory phase while the beam is on (i.e., \( \Psi(t) \rightarrow \Psi \)) and, thus, Equation (17) becomes:

\[
D_{Rx} = \sum_{\text{Phase } k=1}^{P} H(k) \lambda_{Rx}^{k} d_{Rx} \left[ x + u(x, \theta_k) \right] \Psi , I(x, \theta_k) ,
\]

where \( H(k) \) is the heavyside function and equals 1 for phases within the gating window and 0 otherwise. Also, \( \lambda_{Rx}^{k} \) is the fraction of time spent in each respiratory phase during beam-on.
Respiratory gated
Treatment scenario: Dynamic motion compensation

\[ D_{Rx} = \sum_{\text{Phase } k=1}^{p} \lambda_{Rx}^k d_{Rx} \left[ x + u(x, \theta_k) \middle| \Psi_k, I(x, \theta_k) \right], \]
Dynamic compensation
Summary and future directions
Current and future developments

- Audio-visual biofeedback

- Respiratory signal-conditioned acquisition
  - Vedam et al. ASTRO 2005

- 5DF breathing motion model
  - Low et al. IJROBP 2005

- Ventilation assessment
  - Guerrero et al. IJROBP 2005, PMB 2006

- 4D MC calculations
  - Rosu, Heath, Paganetti, Keall, Siebers ...

- 4D CBCT MC calculations
  - HU errors cause both material and density errors
Summary

- Monte Carlo dose calculation has recently seen a resurgence of interest
  - Summer School and other MC workshops
  - AAPM Task Group report
  - Develop, user and vendor progress

- The acquisition and use of 4D data sets during therapy is rapidly advancing
  - Better input data to MC algorithms

- The increased accuracy offered by Monte Carlo and the increased geometric fidelity offered by 4D imaging techniques will allow treatment capabilities and clinical outcome data of unsurpassed quality
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