New Advances in CT: Functional Imaging & Dose Reduction

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Functional Imaging in Radiation Oncology

• Target definition
  – Areas of increased invasiveness and resistance
    • Enhanced angiogenesis
    • Hypoxia
  – GTV, CTV

• Monitoring of tumor response to treatment
  – Tumor mass
  – Reoxygenation
  – Shut down of vasculature
  – Adjuvant chemo and anti-angiogenesis therapy
    • Vascular normalization**

**Jain. Science 307:58, 2005
Functional Imaging Modalities

- Positron Emission Tomography (PET)
- Single Photon Emission Tomography (SPECT)
- Magnetic Resonance Imaging (MRI)
- Computed Tomography?
  - Anatomical/Morphological
- Introduce CT Functional Imaging
  - Brain and liver tumor
- Radiation dose from CT
  - Methods to reduce dose
  - In particular for CT functional imaging
CT Perfusion Brain Tumor Study

**Intravenous Injection of Contrast Agent**
- 40-50 ml @ 3-4 ml/s

**Scan Protocol**
- 80 kVp, 190mA, 4 x 5 mm
- 45 s cine scan
- 1 s every 16 s, 6 times

**Deconvolution**
- CBF ml-min\(^{-1}\) (100g\(^{-1}\))
- CBV ml (100g\(^{-1}\))
- MTT (s)
- PS ml-min\(^{-1}\) (100g\(^{-1}\))
Basis of CT Perfusion (Functional) Imaging

- Tissue curve is dependent on:
  - Blood flow and blood volume
  - Arterial input concentration

Tracer kinetics modeling:
- Models tissue curve with above parameters and arterial concentration
- Fitting of measured tissue curve with model curve
- Estimates of parameters

![Graph showing tissue curve fitting](image)

Mathematical equations:
\[ Q(t) = F \cdot C_a(t) \ast R(t) \]
- \( Q(t) \): Tumor or brain curve
- \( C_a(t) \): Arterial curve
- \( F \): Cerebral blood flow (CBF)
- \( R(t) \): Impulse Residue Function (IRF)
- \( \ast \): Convolution operator
Modeling of Tissue Contrast Kinetics

- **Johnson and Wilson Model**
  - Blood flow, transit time, transcapillary exchange, ven. outflow
  - Exchange regimes
    - Diffusion limited (F << PS); cold xenon
    - Flow limited (F>>PS); intravascular tracer: contrast agent in normal brain
    - Permeable (F ~ PS); contrast agent in most tissues, e.g. liver

*Am J Physiol 210:1299-1303, 1966*
CT Perfusion Imaging in Brain Tumors

- Tissue Blood Flow (CBF, F)
- Tissue Blood Volume (CBV, \( v_b \))
- Microvessel Permeability Surface Area (PS)
- Mean transit time (MTT, \( T_c \))

\[
Q(t) = F \cdot C_a(t) \ast R(t)
\]

\[
PS = -F \ln(1-E)
\]

\[
k = FE/v_e
\]

Validation: Accuracy and Reproducibility

- Rabbit VX2 brain tumor model
- 13% and 7% for CBF and CBV

CT vs. Microspheres CBF Measurements in Brain Tumours

- Tumour
- Peri-Tumour
- Contra-lateral Normal

m = 0.97
r = 0.86

Brain Tumor Studies

- Primary brain tumor – glioma
- Before and 1-2 weeks post radiation therapy
- Changes in CT Perfusion functional parameters and response to treatment
Glioma-2
Glioma-2

- Blood flow map fused with planning CT
- Whole brain irradiation
- 50Gy/25
Glioma-2

Before

After
Glioma-2

Before

After
** Glioma-2

Tumor Regions

** P < 0.05

- ** BF (ml/min/100g)
- ** BV x 10 (ml/100g)
- ** PS x 100 (ml/min/100g)
- ** MTT X 10 (s)

Pre-Treatment
Post-Treatment
Glioma-2

Normal Regions

** P < 0.05

- BF (ml/min/100g)
- BV x 10 (ml/100g)
- PS x 100 (ml/min/100g)
- MTT X 10 (s)

- Pre-Treatment
- Post-Treatment
Glioma-2
CT Liver Perfusion Study

\[ Q(t) = F \cdot [\alpha \cdot C_a(t) + (1 - \alpha) \cdot C_p(t)] \cdot R(t) \]

- \( Q(t) \): Tumor or liver curve
- \( C_a(t) \): Aortic curve
- \( C_p(t) \): Portal venous curve
- \( F \): Total hepatic blood flow (BF)
- \( \alpha \): Hepatic arterial fraction (HAF)
- \( R(t) \): Impulse Residue Function (IRF)
CT Liver Perfusion Study

- Couch ‘shuttles’ free breathing patient between two locations
- Each location is scanned every 2.8 s
- 8 x 5 mm thick slices for each location
- Total 80 mm coverage with 16 x 5 mm slices
- Images have to be sorted to reduce patient motion
CT Liver Perfusion Study

Unsorted

Sorted

Aorta

Portal Vein
CT Liver Functional Maps

Total Liver Blood Flow
(ml min⁻¹ (100g)⁻¹)

Hepatic Arterial Fraction (HAF)
(% Total Blood Flow from Artery)

- Metastasis was more hypovascular than surround normal liver tissue
- Does it mean that the metastasis was hypoxic?
Hepatic Arterial Blood Flow (ml·min\(^{-1}\)·(100g\(^{-1}\))

Total Blood Flow

HAF

CT Liver Functional Maps

- Hepatic arterial blood flow (HAF) in metastasis is greater than or equal to that in normal liver tissue.
- Metastasis might not be hypoxic, particularly in the rim.
- Indicates feasibility of radiation treatment for liver tumor?
Validation of CT Liver Perfusion

- Seven New Zealand White Rabbits with implanted VX2 tumor in the liver

![Graph showing DCE-CT HBF vs Microsphere HBF with regression line: $CTP = 0.92 \text{ MS} + 4.62$, $R^2 = 0.81$.]

Stewart & Lee. PMB 53:4249, 2008
CT Liver Perfusion Study

- **Objective**
  - CT Perfusion functional parameters to distinguish tumor from normal tissue

- 7 Hepatocellular Carcinoma (HCC), 5 metastases and 1 cholangioma

- Each subject had a CT Perfusion Liver study with the free breathing axial shuttle technique

- 120 kVp, 60 mAs, 0.4 s rotation period, 42 passes of the axial shuttle with the first 4 as baseline

- 60 – 70 ml of Omnipaque 300 injected at 3 ml·s\(^{-1}\) at the 5\(^{th}\) pass of the axial shuttle
CT Liver Perfusion Study

• Results
  – Total blood flow was lower while arterial blood flow was higher in the tumor than in normal tissue
  – Tumor may not be hypoxic

- **Hepatic Arterial Fraction (%)**

- **Total Blood Flow (ml/min/100g)**

- **Arterial Blood Flow (ml/min/100g)**
CT Radiation Dose

- NCRP Report 160 – Ionizing Radiation Exposure of the Population of the US
  - 2006
    - 414 million X-ray procedures
      - 62 million CTs (15%)
    - Collective radiation dose
      - 900,000** person-Sv (vs 124,000 in 1990)
      - 918,000 person-Sv from background
      - 440,000 person-Sv from CT

** From all ionizing radiation procedures including Nuclear Medicine and therapy

NEJM 357:2277, 2007
## CT Radiation Dose

- **Typical effective dose of CT studies**

<table>
<thead>
<tr>
<th>CT Scan</th>
<th>UK 2003**</th>
<th>Europe 2004**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DLP (mGy-cm)</td>
<td>Effective Dose (mSv)</td>
</tr>
<tr>
<td>Routine Head</td>
<td>931</td>
<td>2.0</td>
</tr>
<tr>
<td>Abdomen (Liver metastases)</td>
<td>472</td>
<td>7.1</td>
</tr>
<tr>
<td>Chest, abdomen &amp; pelvis (lymphoma staging or follow up)</td>
<td>937</td>
<td>14.1</td>
</tr>
<tr>
<td>Chest (lung cancer: known, suspected or metastases)</td>
<td>575</td>
<td>8.1</td>
</tr>
</tbody>
</table>

**Shrimpton et al. NRPB-W67, 2005**

<table>
<thead>
<tr>
<th>CT Functional Study</th>
<th>DLP (mGy-cm)</th>
<th>Effective Dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head (4 cm)</td>
<td>2289</td>
<td>4.8</td>
</tr>
<tr>
<td>Liver (axial shuttle – 8 cm)</td>
<td>1268</td>
<td>19.0</td>
</tr>
</tbody>
</table>
CT Dose Reduction – mA Modulation

a) with patient size (adult vs children)

b) according to patient thickness along longitudinal (z) axis

c) according to patient thickness in the transaxial plane

d) Combination of a), b) and c)

e) Dose shield for helical scan
CT Dose Reduction

- mA modulation in the transaxial plane
- Dose reduction 22 – 34% **

Kalra et al. Radiology 233:649, 2004

CT Dose Reduction

- mA modulation along longitudinal (z) axis
- Dose reduction by 32% on average

CT Dose Reduction

- Beam collimation to reduce overscan in axial direction
- Dose reduction by 13-36\%**

**Tzedakis et al. Med Phys 32:1621, 2005

Carrington; Somaton Sessions 22:6, 2008
CT Dose Reduction

- Adaptive Statistical Iterative Reconstruction (ASIR)
Dose Reduction by ASIR

- Liver scan – portal phase

w/o ASIR
DLP: 836 mGy-cm

w ASIR
DLP: 688 mGy-cm
18% less
Dose Reduction by ASIR

- Brain scan

w/o ASIR
DLP: 1018 mGy-cm

w ASIR
DLP: 939 mGy-cm
8% less
Dose Reduction by ASIR

- **Brain Functional Study**
  - 4 patients recruited
  - Each patient had a high dose and low dose CT Perfusion studies separated by 10 min
  - High and low dose study used 200 and 50 mAs per image
  - The low dose study was also processed by ASIR

---

80 kVp 200 mAs

80 kVp 50 mAs

80 kVp 50 mAs + ASIR
Dose Reduction by ASIR

- Brain Functional Study: Average Map

80 kVp 200 mAs

80 kVp 50 mAs

80 kVp 50 mAs + ASIR
Dose Reduction by ASIR

- Brain Functional Study

80 kVp 200 mAs

80 kVp 50 mAs

80 kVp 50 mAs + ASIR

Blood Flow

Blood Volume
Dose Reduction by ASIR

- Figure of Merit (FOM) of Functional Maps
  - Segment out grey and white matter
  - Grey and white matter pixel mask on functional maps
  - Mean (μ) and standard deviation (σ) of functional parameter
  - \[ \text{FOM} = \frac{\sigma}{\mu} \]
Dose Reduction by ASIR

- Figure of Merit (FOM)

**White Matter Blood Flow**

- High Dose
- Low Dose
- LD+ASIR

**White Matter Blood Volume**

- High Dose
- Low Dose
- LD+ASIR

P < 0.05
Dose Reduction by ASIR

- Figure of Merit (FOM)

Grey Matter Blood Flow

Grey Matter Blood Volume

P < 0.05
## Comparison of Functional Imaging Modalities

<table>
<thead>
<tr>
<th>Features</th>
<th>MR</th>
<th>CT</th>
<th>PET</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speed</strong></td>
<td>√√</td>
<td>√√√</td>
<td>√√</td>
<td>√</td>
</tr>
<tr>
<td><strong>Resolution</strong></td>
<td>√√</td>
<td>√√√</td>
<td>√√√</td>
<td>√</td>
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<tr>
<td><strong>Axial coverage</strong></td>
<td>√√</td>
<td>√√√</td>
<td>√√√</td>
<td>√√√</td>
</tr>
<tr>
<td><strong>Radiation dose</strong></td>
<td>no</td>
<td>xx</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td><strong>On-site cyclotron</strong></td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td><strong>Quantification</strong></td>
<td>√√√</td>
<td>√√√</td>
<td>√√√</td>
<td>√</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>x x</td>
<td>x</td>
<td>x x x</td>
<td>x x x</td>
</tr>
</tbody>
</table>
Conclusion

- CT Perfusion (Functional) imaging is an easy extension of routine contrast enhanced CT scanning
- Based on ‘realistic’ modeling of transport kinetics of blood-borne contrast agents
- Blood flow is validated against microspheres
- Define targets for radiation treatment
- Monitor progress and treatment response of tumors
- With new radiation dose reduction techniques, viable alternative to PET and MR
Dose Reduction by ASIR

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  - 4 patients recruited
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80 kVp 20 mAs

80 kVp 20 mAs + ASIR
Dose Reduction by ASIR

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Dose Reduction by ASIR

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Blood Flow

Blood Volume
Dose Reduction by ASIR

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  - Segment out grey and white matter
  - Grey and white matter pixel mask on functional maps
  - Mean ($\mu$) and standard deviation ($\sigma$) of functional parameter
  - $\text{FOM} = \frac{\sigma}{\mu}$
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D Ouimet  L Desjardins
M Murphy  F Su
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