Functional CT and MRI

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Functional imaging in oncology

- Metabolism
  - PET, MRS
  - SUV
  - Cho.
- Tumor biology
- Vascularity
  - Perfusion
  - $K^\text{trans}$
- Cellularity
  - Diffusion
  - ADC
Perfusion Imaging
Vascularity: normal vessel vs tumor vessel

- Blood vessel volume
- Integrity of endothelial junction, O2 pressure

Blood flow
Permeability
O2 pressure
Interstitial Pr

Nat Med 2003; 9: 713
Emerging aspect of cancer care

Angiogenesis as a therapeutic target

Napoleone Ferrara¹ & Robert S. Kerbel²

Inhibiting angiogenesis is a promising strategy for treatment of cancer and several other disorders, including age-related macular degeneration. Major progress towards a treatment has been achieved over the past few years, and the first antiangiogenic agents have been recently approved for use in several countries. Therapeutic angiogenesis (promoting new vessel growth to treat ischaemic disorders) is an exciting frontier of cardiovascular medicine, but further understanding of the mechanisms of vascular morphogenesis is needed first.
HCC treated with Avastin
Perfusion Imaging

Dynamic data acquisition c high temporal resolution

Time curve

\[ C_t(t) = K_{\text{trans}} [C_p(t) \otimes e^{(-k_{\text{ep}} t)}] + v_p C_p(t) \]
Perfusion CT before and after treatment with Avastin in HCC

Blood flow

Before: (82 mL/100g/min)

After: (20 mL/100g/min)

Blood volume

Before: (5.4 mL/100g)

After: (1.4 mL/100g)
Advanced HCC: CT perfusion of liver and tumor tissue—Initial experience

### CT Perfusion Parameters of Primary HCC, Background Liver, and Spleen

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HCC</th>
<th>Background Liver</th>
<th>Spleen</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BF (mL/100 g/min)</td>
<td>92.8 ± 88.6</td>
<td>14.9 ± 2.8</td>
<td>124.9 ± 84</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BV (mL/100 g)</td>
<td>4.9 ± 3.5</td>
<td>2.6 ± 0.9</td>
<td>5.8 ± 2.3</td>
<td>.004</td>
</tr>
<tr>
<td>MTT (sec)</td>
<td>8.1 ± 3.1</td>
<td>14.9 ± 2.3</td>
<td>6.2 ± 3.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PS (mL/100 g/min)</td>
<td>34.5 ± 11.9</td>
<td>23.5 ± 8.2</td>
<td>40.9 ± 15.5</td>
<td>.001</td>
</tr>
</tbody>
</table>

Note.—Data are means ± standard deviations.
* A P value of ≤.05 indicates a significant difference between any two of the three regions (HCC, liver, or spleen).

### CT Perfusion Parameters of Grades of HCC

<table>
<thead>
<tr>
<th>Grade</th>
<th>BF (mL/100 g/min)</th>
<th>BV (mL/100 g)</th>
<th>MTT (sec)</th>
<th>PS (mL/100 g/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well differentiated (n = 9)</td>
<td>173.4 ± 106.6</td>
<td>7.8 ± 4.5</td>
<td>5.8 ± 2.7</td>
<td>44.5 ± 13.3</td>
</tr>
<tr>
<td>Moderately differentiated (n = 11)</td>
<td>42.4 ± 14.6</td>
<td>3.1 ± 0.6</td>
<td>9.7 ± 2.1</td>
<td>27.9 ± 5.3</td>
</tr>
<tr>
<td>Poorly differentiated (n = 5)</td>
<td>58.1 ± 26.3</td>
<td>3.5 ± 0.6</td>
<td>8.7 ± 3.3</td>
<td>30.9 ± 7.4</td>
</tr>
<tr>
<td>P value*</td>
<td>.001</td>
<td>.003</td>
<td>.01</td>
<td>.002</td>
</tr>
</tbody>
</table>

Note.—Data are means ± standard deviations.
* A P value of ≤.05 indicates a significant difference between any two of the three grades.
Perfusion value: Early monitoring

Before CCRT

Blood flow: 313
Blood volume: 25
Permeability: 27

1M after CCRT

Blood flow: 184
Blood volume: 11
Permeability: 11
Perfusion value: Early monitoring

Before CCRT

Blood flow
Blood volume
Permeability

1M after CCRT

Perfusion value: Early monitoring
Perfusion CT: Prediction of response before treatment

- High perfusion
- More oxygen & drug delivery
- Increased radiosensitizing & cytotoxic effect
- Good response

A higher $K_{\text{trans}}$ in responders c pancreatic ca. after CCRTx

Park MS. Radiology. 2009
Perfusion CT

- Quantification: Blood flow, Blood vol, Permeability, Mean transit time

- Tumor grading, treatment response, early monitoring, prediction of prognosis

- Radiation
Perfusion MRI

- Quantification: $K^{\text{trans}}, K_{\text{ep}}, V_e, \text{AUC}$

- Non-linear correlation: contrast concentration and MR signal

- No radiation

- Multi-parametric evaluation
**Imaging Guidelines for Clinical Trials**


**Fluorodeoxyglucose PET (FDG PET)** - guidelines resulted from the NCI CIP workshop convened on January 10-11, 2005, in Washington, DC.
ABSTRACT

Background. This study utilized the imaging data of primary liver cancer (PLC) treated with fluorouridine (FUDR) and bevacizumab to test the hypothesis that dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) parameters correlate with tissue hypoxia markers and treatment outcome.

Methods. Seventeen patients with PLC were treated with hepatic artery infusional (HAI) FUDR for 14 days followed by systemic bevacizumab therapy. DCE-MRI images were obtained at baseline and after HAI FUDR and bevacizumab therapy. The parameters ($K_{\text{trans}}$, AUC) pertaining to perfusion and vascular permeability of the tumor and adjacent liver parenchyma were measured with DCE-MRI. Tissue obtained at baseline was stained for hypoxia inversely with changes in AUC90 and AUC180 after bevacizumab ($P = 0.002$ and $P = 0.0001$). Reductions in tumor perfusion (AUC90 and AUC180) were greater in tumors expressing anti-hypoxia inducible factor-1z ($P = 0.02$ and 0.03), vascular endothelial growth factor ($P = 0.01$ and $P = 0.01$), and anti-carbonic anhydrase IX ($P = 0.009$ and $P = 0.009$).

Conclusions. In patients with PLC, bevacizumab induces a reduction in tumor perfusion measured by DCE-MRI. These changes correlate with TTP and tissue markers of tumor hypoxia.

Tumor response to cytotoxic chemotherapy is typically measured on cross-sectional imaging using either the Response Evaluation Criteria in Solid Tumors (RECIST) or

- Bevacizumab induces a reduction in tumor perfusion in DCE MRI.
- These changes correlate with TTP and tumor markers of tissue hypoxia.
Antiangiogenic Agents

- Blocking VEGF or VEGFR -> Normalization of abnormal vessel
- Potentiate effects of CTx & RTx
- Delicate balance between too many and too few endothelial cells
- Optimal schedule for combination therapy

Response of metastasis: Avastin

Baseline
K trans 0.121

Avastin #3
0.022

Avastin #7
0.043

Avastin #14
0.096
Response of metastasis: $K_{\text{trans}}$
Dynamic contrast-enhanced MRI as a predictor of tumour response to radiotherapy

Mark A Zahra, Kieren G Hollingsworth, Evis Sala, David J Lomas, Li T Tan

A predictive technique in the management of patients with cancer could improve the therapeutic index by allowing...
Diffusion MRI
Diffusion in tissue

Restricted diffusion

- High cellularity
- Intact cell membrane

Free diffusion

- Low cellularity
- Defective cell membrane

- Koh et al. AJR 2007; 188:1622-1635
Signal intensity on DWI and ADC map

B=0  B=300  B=600  B=900  ADC map

Cyst  Mets

Slope = ADC

Free diffusion

Restricted diffusion

Courtesy from Lee SS
## Detection Rate of FLLs in 53 Patients with DW and T2-weighted MR Imaging

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Lesions ($n = 211$)</th>
<th>Malignant Lesions ($n = 136$)</th>
<th>Benign Lesions ($n = 75$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DW imaging</td>
<td>87.7 (185/211)</td>
<td>86.4 (117.5/136)</td>
<td>90.0 (67.5/75)</td>
</tr>
<tr>
<td>T2-weighted imaging</td>
<td>70.1 (148/211)</td>
<td>62.9 (85.5/136)</td>
<td>83.3 (62.5/75)</td>
</tr>
<tr>
<td>$P$ value</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.03</td>
</tr>
</tbody>
</table>

*Note.—Data are averaged for two independent observers. Unless otherwise indicated, numbers are percentages, with raw data in parentheses.*
Diagnostic performance of apparent diffusion coefficient for predicting histological grade of hepatocellular carcinoma

Akihiro Nishie, Tsuyoshi Tajima, Yoshiki Asayama, Kousei Ishigami, Daisuke Kakhara, Tomohiro Nakayama, Yukiisa Takayama, Daisuke Okamoto, Nobuhiro Fujita, Akinobu Taketomi, Kengo Yoshimitsu, Hiroshi Honda


High-b-Value Diffusion-Weighted MR Imaging of Hepatocellular Lesions: Estimation of Grade of Malignancy of Hepatocellular Carcinoma

Ali Muhi, MD, Tomoaki Ichikawa, MD, Utaro Motosugi, MD, Katsuhiro Sano, MD, Masanori Matsuda, MD, Takatoshi Kitamura, MD, Tadao Nakazawa, MD, and Tsutomu Araki, MD


Diffusion-Weighted Imaging of Surgically Resected Hepatocellular Carcinoma: Imaging Characteristics and Relationship Among Signal Intensity, Apparent Diffusion Coefficient, and Histopathologic Grade

Korean J Radiol 2010; 11: 295-303
Histologic grading of 201 HCCs: DWI vs arterial enhancement vs EOB-uptake

<table>
<thead>
<tr>
<th></th>
<th>well</th>
<th>moderately</th>
<th>poorly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative on DWI and AP</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Positive on one of them</td>
<td>10</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Positive on DWI and AP</td>
<td>14</td>
<td>120</td>
<td>33</td>
</tr>
</tbody>
</table>
Well vs Poorly differentiated HCC
DW MRI: A biomarker for Tx response

Diffusion Magnetic Resonance Imaging: A Biomarker for Treatment Response in Oncology

Daniel A. Hamstra, Alnawaz Rehemtulla, and Brian D. Ross

Meeting Report

Diffusion-Weighted Magnetic Resonance Imaging as a Cancer Biomarker: Consensus and Recommendations

DW MRI: A biomarker for Tx response

Solid cellular tumor
- Effective Therapy

Microscopic cellular necrosis

Necrotic tissue
Correlation between Diffusion, perfusion, and glucose metabolism in 31 advanced HCCs

SUV and ADC

SUV and $K^{\text{trans}}$
Responder vs non-responder in HCCs with CCRTx: Diffusion, perfusion, and glucose metabolism

SUV

ADC

\[ \text{ADC} \]

\[ K_{\text{trans}} \]
Diffusion MR

• Cellularity
• No contrast agent
• Scan time: technical-depend
• Wide coverage
• Simple equation
• Automatic quantification

Perfusion MR

• Vascularity
• Contrast agent
• Scan time: physiology-depend
• Narrow coverage
• Complicated equation
• No automatic quantification
Current application

**DWI MR**
- Daily practice
- Research base

**DCE MR**
- Research base
- Daily practice?
Conclusion

- Quantification
- Oncologic application: detection, characterization, grading, treatment response, prediction
- Lack of standard absolute value
- Research-based application