Diffusion MRI of bone marrow in health and oncologic disease

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SCBT/MR 2016
51 yo female with metastatic breast cancer. Rx Erubulin chemotherapy. No G-CSF.

What is the response between Baseline → Ex2 Ex2 → Ex3?

A. Response → Response
B. Progression → Progression
C. Response → Progression
D. Progression → Response
E. Can’t tell → won’t tell
51 yo female with metastatic breast cancer. Rx Erubulin chemotherapy. No G-CSF.
What is the response between Baseline $\rightarrow$ Ex2 then Ex2 $\rightarrow$ Ex3?

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<thead>
<tr>
<th>Date</th>
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<tr>
<td>16Jan14</td>
<td>Baseline</td>
<td>14May14</td>
<td>x6 Erubulin</td>
<td>08Sept14</td>
<td>x12 Erubulin</td>
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x6 Erubulin

08Sept14
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Biological processes involved in therapy induced changes in DWI

Siemens Oncotreat Software, WIP

C. Response $\rightarrow$ Progression

Normal bone marrow

- Hematopoietic organ: produces ≈ 500 billion blood cells/day
- 4% of total body mass of adult humans
- Adult BM distribution established by 25 yo
- Age related changes occur in bone and bone marrow
  - Trabecular bone loss & increased fat (>40 yo [>♀])
  - Decreases in cellularity/synthetic function; starts in 5th-6th decades
  - Reticulin/collagen increases with age
Proliferation, migration, and invasion of cancer cells in BM displaces fat & normal myeloid and erythroid cells.
Osteoblasts: Bone scans, NaF-PET, CT

Bone trabeculae & osteoclasts: CT scans (qCT), UTE-MRI, FDG-PET, R2*

Vascularity: DCE-MRI

Cell density: DW-MRI
Fat water imaging: Dixon MRI, MRS, CT

Tumor cell surface & cytoplasmic receptors (specific): F-DHT, FES, labelled antibodies/pharmacophores to PSA, Ga/F-PSMA, HER2-neu

Tumor metabolism (non-specific): FDG, choline, acetate & methionine-PET

Fat cells

Normal myeloid, erythroid precursor & stromal cells

DWI enhances specificity to tumor in BM

75 yo with metastatic breast cancer
What b-value choice for whole body MRI?

- What water compartment is being studied?
  - Minimize perfusion & susceptibility effects and maximize sensitivity to BM cellular content
- Outline of body should be retained to enable registration of images to anatomy sequences
- Image distortions need to be minimized
- Need to evaluate normal/pathologic soft tissues also (liver, nodes etc)
- Need to maximize tumor-bone marrow CNR
- Yield reliable estimates of ADC

DWI is an integral part of whole body assessments (Eyes to thighs in 50 mins; 4500 images!)
WB-DWI sub-protocol
(STIR for FS – total 25mins)

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<td>min (68)</td>
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<tr>
<td>NE</td>
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<td>Scan time/station (mins)</td>
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Normal bone marrow on DWI

- Age related changes in bone and bone marrow are reflected on high b-value DWI
  - Trabecular bone loss & increased BM fat (>40 yo [♀])
  - Decreases in BM cellularity with age
  - BM (reticulin/collagen) increases with age

Variability within same age group

17 yo 29 yo 45 yo 57 yo 67 yo
Bone marrow hyperintensity on DWI (=hypercellularity)

- Malignant infiltration
- Children & young adults
- Primary or secondary polycythemia
  - High altitude living and athletes
  - Pregnant or recently pregnant
  - Hypoxia associated: smoking, COPD, obstructive sleep disease (obesity)
  - Chronic cardiac failure
  - Neoplastic – RCC, HCC, VHL disease, pheochromocytoma, functional adrenal adenomas
  - Drugs – anabolic steroids, erythropoietin
- Rebound/recovery after BM toxic Rx
- Granulocyte-Colony Stimulating Factors (G-CSF/GM-CSF therapy)

<table>
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<th>Lactating</th>
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26 yo H/O melanoma on surveillance
Factors affecting BM cellularity-ADC relationships

- Blood flow is highest in malignant marrow
- Extracellular space water is greater for mixed red marrow
- Fat cells impede water motions > hemopoietic cells
  - Fat cells are 50-65 µm in diameter (≈65,000 µm³)
  - Hemopoietic cells 5-15 µm in diameter (≈525 µm³)
- b-values <1000 s/mm², sensitivity to slow intracellular water ↓
Non-linear, positive (paradoxical) relationship between ADC & bone marrow cellularity

- **Yellow (fatty) marrow** → low DW SI & ADC
  - Many large fat cells & few smaller cells
  - Low water content & cellularity
  - Fat acts as a repellent to water
  - Low perfusion

- **Red bone marrow** → higher DW SI & ADC
  - Less big fat cells & more smaller cells
  - More water within & outside cells
  - Larger extracellular water fraction
  - Higher perfusion

- **Tumor & BM hyperplasia** → highest DW SI but **variable** ADC
  - Highest cellularity within restricted bone marrow space (increased tortuosity)
  - Smaller extracellular water fraction
  - Highest perfusion

BM hypointensity on DWI
Bone marrow b900 SI decreases with chemotherapy
25F – Metastatic malignant ovarian teratoma. Pre & Post x3 BEP
Left breast cancer – changes in normal marrow on adjuvant endocrine Rx (letrozole)
Changes in normal marrow on adjuvant letrozole

$b900$ SI ↓
$ADC$ (677 → 676 $\mu$m$^2$/s) ↔
$F\%$ (42 → 49) ↑
Iron overload and marrow signal intensity

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Hardware factors and bone marrow signal intensity

Field strength & coil design effects

1.5T Avanto
x4 50cm stations

1.5T AvantoFit
x4 50cm stations

3T PrizmaFit
x4 50cm stations

1.5T AvantoFit
x4 60cm stations

51 yo. Metastatic breast cancer. Rx TDM-1 in complete response.
Summary: causes of bone marrow intensity changes on high b-value images

- BM Hyperintensity
  - ↑ BM fat with ↓ trabecular bone thickness (normocellularity)
  - ↑ ↑ matrix calcification/ossification/ trabecular bone thickness

- BM Hypointensity
  - ↑ BM iron & collagen

- BM hypercellularity
  - ↑ ↑ ↑ matrix calcification/ossification/ trabecular bone thickness