Functional liver image guided hepatic therapy (FLIGHT) with hepatobiliary iminodiacetic acid (HIDA) scans

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Assessments of Global Liver Function

- The gold standard indocyanine green retention at 15 minutes (ICGR15)
- Child-Trucotte-Pugh (CTP) score
- Model for end-stage liver disease (MELD) score
- Albumin-bilirubin (ALBI) score
Assessments of Global Liver Function

ICG-R15

NO Regional Information

CTP score

ALBI score

MELD score

Liver Functions

Removes potentially toxic byproducts of certain medications.

Prevents shortages of nutrients by storing vitamins, minerals and sugar.

Helps your body fight infection by removing bacteria from the blood.

Produces bile, a compound needed to digest fat and to absorb vitamins A, D, E and K.

Helps synthesize proteins needed for growth and repair.

Produce energy, when needed.

Regulate blood clotting.
Hepatobiliary iminodiacetic acid (HIDA) scans

- $^{99m}$Tc iminodiacetic acid analogues are a group of radiopharmaceuticals which are taken up by hepatocytes and excreted into the biliary tract similar to bilirubin
- Used to demonstrate the distribution of functioning hepatic tissue
HIDA scans

- Provide global and regional assessments of liver function
- Can serve as a road map for functional avoidance in treatment planning
- Correlate well with the gold standard ICG-R15*

* Erdogan et al, Liver International 2004, 24, 117-123
HIDA Scan Protocol

- 85 MBq Tc99m-mebrofenin injected
- Dynamic images obtained after an hour, over a 6 min period by dual-headed gamma camera

Global HIDA Value = Rate of liver uptake between 150–300 s

Body surface area
HIDA Images
Global HIDA Value

- HIDA images alone give relative values in different regions and are lack of interindividual comparability
- Global HIDA value corrects for variations in the global function and can improve interindividual comparisons
- Global HIDA Value* = \[
\frac{\text{Rate of liver uptake between 150–300 s}}{\text{Body surface area}}
\]
- Unit - %/min/m²

* Long et al, Practical Radiation Oncology (2018) 8, 429-436
High Value in Bile Duct

- HIDA travels through bile duct and gives a high value in bile duct.
Bile Duct Mask

Masked to background liver uptake
Contouring the Functional Areas

- HIDA scan was fused to the planning computed tomography with contours generated from percent of maximum
Contouring the Functional Areas

- Contour the functional areas (% of max value)
  - 0 - 25%
  - 25 - 50%
  - 50 - 75%
  - 75 - 100%
FLIGHT Planning

- Functional liver image guided hepatic therapy planning (FLIGHT)
- Primary goal of FLIGHT planning was to maximize the functional residual capacity (FRC) of the liver.
- Minimize dose to the highest functioning liver (HIDA uptake 50% - 100% max)
- To preferentially distribute dose through the regions of the liver with a lower function.
FLIGHT Planning

- Typical prescribed dose 8Gy × 5.
- Provided equivalent target coverage to standard SBRT plans
- >98% of gross tumor volume (GTV) covered by 110% of the prescribed dose
- >95% of the planning target volume (PTV) covered by 100% of the prescribed dose
- Without increasing organ at risk (OAR) doses above standard published thresholds
FLIGHT vs Standard SBRT

- Beam Arrangements

**Standard SBRT**

**FLIGHT SBRT**
**Optimization**

- Tighter constraints on higher functional area

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FLIGHT vs Standard SBRT

- Spare high functional area
FLIGHT vs Standard SBRT - DVHs

- Standard SBRT
- FLIGHT SBRT
Functional DVH (fDVH)

- Traditional DVH does not consider the functional competence of different regions.* (Duke University)
- The functional dose–volume histogram is a variation of the dose–volume histogram (DVH), which incorporates the non-uniform distribution of functional subunits into the dose–volume consideration.** (University of Chicago)

**DVH vs fDVH**

- **DVH (assume uniform function distribution)**

- **fDVH (Nonuniform function distribution)**
Functional DVH

\[ f_{DVH}(D_0) = \frac{\text{number of functional units receiving at least the dose } D_0}{\text{total number of functional units}} \]

\[ f_{DVH}(D_0) = \frac{\int_{V_0} dr f(r) \Theta(D(r) - D_0)}{\int_{V_0} dr f(r)} \]

\[ \Theta(D(r) - D_0) \text{ is the step function which is 1 when } D(r) > D_0 \text{ and 0 when } D(r) < D_0 \]

**Absolute fDVH**

- **Absolute fDVH**($D_0$) = % fDVH($D_0$) $\times$ Global HIDA Value
- **Global HIDA Value** =

  
  \[ \text{Rate of liver uptake between 150–300 s} \]

  \[
  \text{Body surface area}
  \]
DVH and fDVH for normal vs FLIGHT SBRT

- % fDVH
- Absolute fDVH

Global HIDA Value: 4.98%/min/m²
FRC\textsubscript{15} HIDA

- Functional residual capacity < 15 Gy
- \(\text{FRC}_{15} \text{ HIDA} = (\% \text{counts} < 15 \text{ Gy}) \times \text{ (Global HIDA)}\)*
- Represents the liver functionally spared from radiation, receiving below 15 Gy
- 15 Gy was extrapolated from a volumetric parameter evaluated at our institution**
- Close to what suggested from MR perfusion data, 17 Gy (University of Michigan)***

* Long et al, Practical Radiation Oncology (2018) 8, 429-436
** Lasley et al, Practical Radiation Oncology (2015) 5, e443-e449
FRC\textsubscript{15} HIDA for normal vs FLIGHT SBRT

- Functional residual capacity < 15Gy
- FLIGHT SBRT
- normal SBRT
- FRC\textsubscript{15} HIDA for FLIGHT is 3.76
- FRC\textsubscript{15} HIDA for normal SBRT is 3.15
Equivalent uniform dose (EUD) and functional EUD (fEUD)

The concept of equivalent uniform dose (EUD) assumes that any two dose distributions are equivalent if they cause the same radiobiological effect.*

\[ EUD = \left( \frac{\sum_{i=1}^{N} \nu_i D_i^a}{\sum_{i=1}^{N} \nu_i} \right)^{1/a} \] **

\( a \) was calculated using \( TD_{5/5}(1) = TD_{5/5}(v) v^{1/a} \)

* Niemierko, Medical Physics 24, 103, 1997
EUD and fEUD

- To calculate fEUD, replace the volume weighting with function weighting in EUD formalism. *
- The tumour and critical structures activity/function can be incorporated in calculation

\[
FEUD = \left( \frac{\sum_{i=1}^{N} f_i D_i^a}{\sum_{i=1}^{N} f_i} \right)^{1/a}
\]

### FLIGHT vs normal SBRT

<table>
<thead>
<tr>
<th>Metric</th>
<th>Standard</th>
<th>FLIGHT</th>
<th>Relative Improvement</th>
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<tr>
<td>FRC$_{15}$HIDA (%/min/m²)</td>
<td>3.15</td>
<td>3.76</td>
<td>19.40%</td>
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<tr>
<td>Mean Liver Dose (Gy)</td>
<td>15.11</td>
<td>12.55</td>
<td>16.90%</td>
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<td>EUD</td>
<td>22.02</td>
<td>21.26</td>
<td>3.40%</td>
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<td>FEUD</td>
<td>20.59</td>
<td>19.33</td>
<td>6.10%</td>
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**Global HIDA Value:** 4.98%/min/m²

**15 Gy**
FLIGHT vs normal SBRT - statistics

- $FRC_{15}$ HIDA, liver dose, EUD, fEUD were compared for 17 patients

<table>
<thead>
<tr>
<th></th>
<th>Standard (n = 17)</th>
<th>FLIGHT (n = 17)</th>
<th>Mean relative improvement (Range)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Mean $FRC_{15}$ HIDA (%/min/m²)</td>
<td>2.48</td>
<td>2.63</td>
<td>5.3% (1.2-20.2%)</td>
<td>.012</td>
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<tr>
<td>Mean liver dose (Gy)</td>
<td>9.07</td>
<td>7.89</td>
<td>14.7% (0.9-33.6%)</td>
<td>&lt;.001</td>
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<tr>
<td>Mean EUD</td>
<td>16.14</td>
<td>15.15</td>
<td>6.2% (−0.2 to 16.6%)</td>
<td>&lt;.001</td>
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<tr>
<td>Mean FEUD</td>
<td>16.14</td>
<td>14.89</td>
<td>7.9% (0.04-18.7%)</td>
<td>&lt;.001</td>
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<td>Gradient index</td>
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EUD, equivalent uniform dose; FEUD, functional equivalent uniform dose; FLIGHT, functional liver image guided hepatic therapy; $FRC_{15}$, amount of function <15 Gy; HIDA, hepatobiliary iminodiacetic acid
Acknowledgement

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Questions