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

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INDIANA UNIVERSITY
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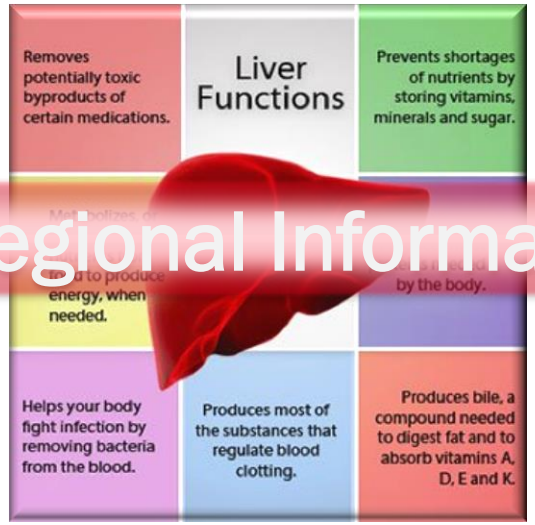
Assessments of Global Liver Function

- 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

Assesments of Global Liver Function

ICG-R15

ALBI score



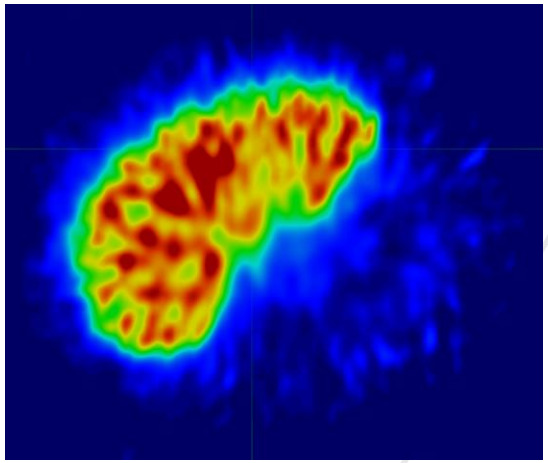
NO Regional Information

CTP score

MELD score

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



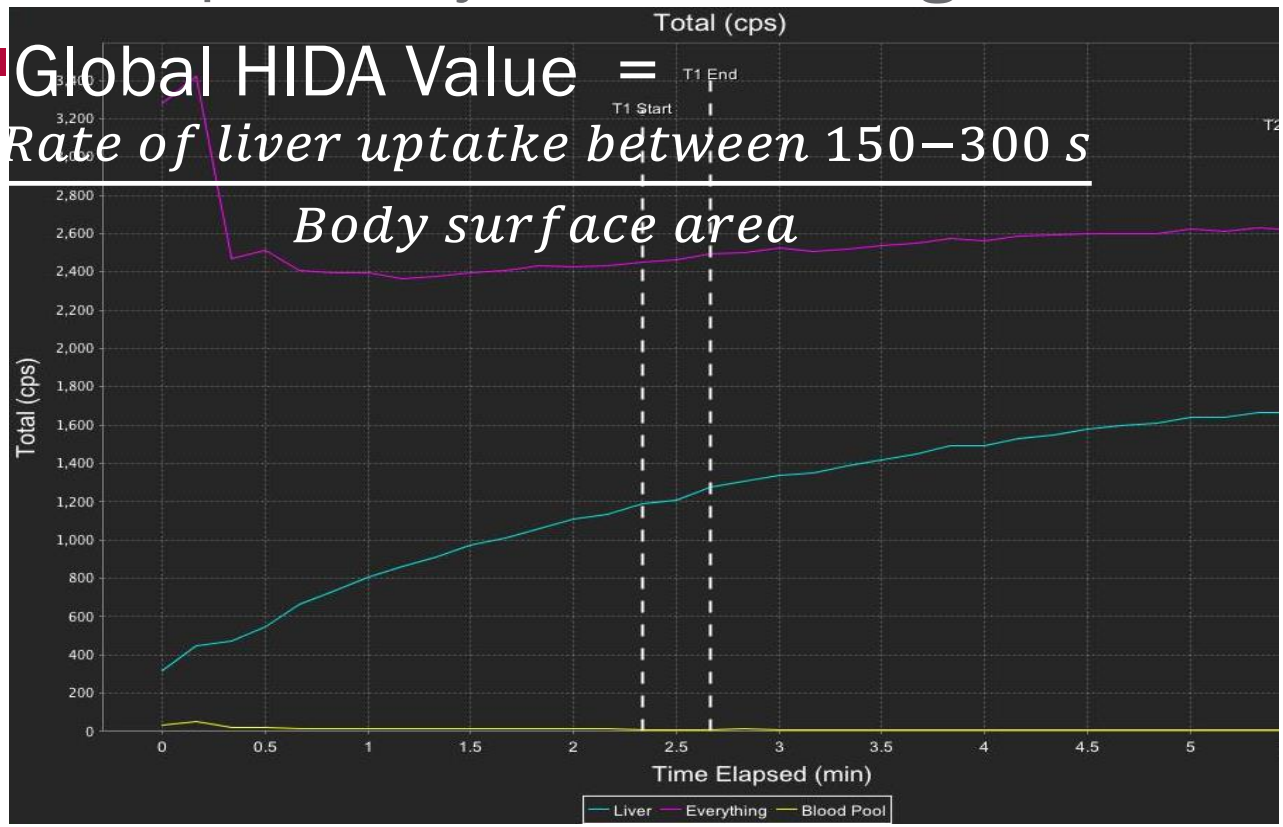
HIDA scans

- 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*

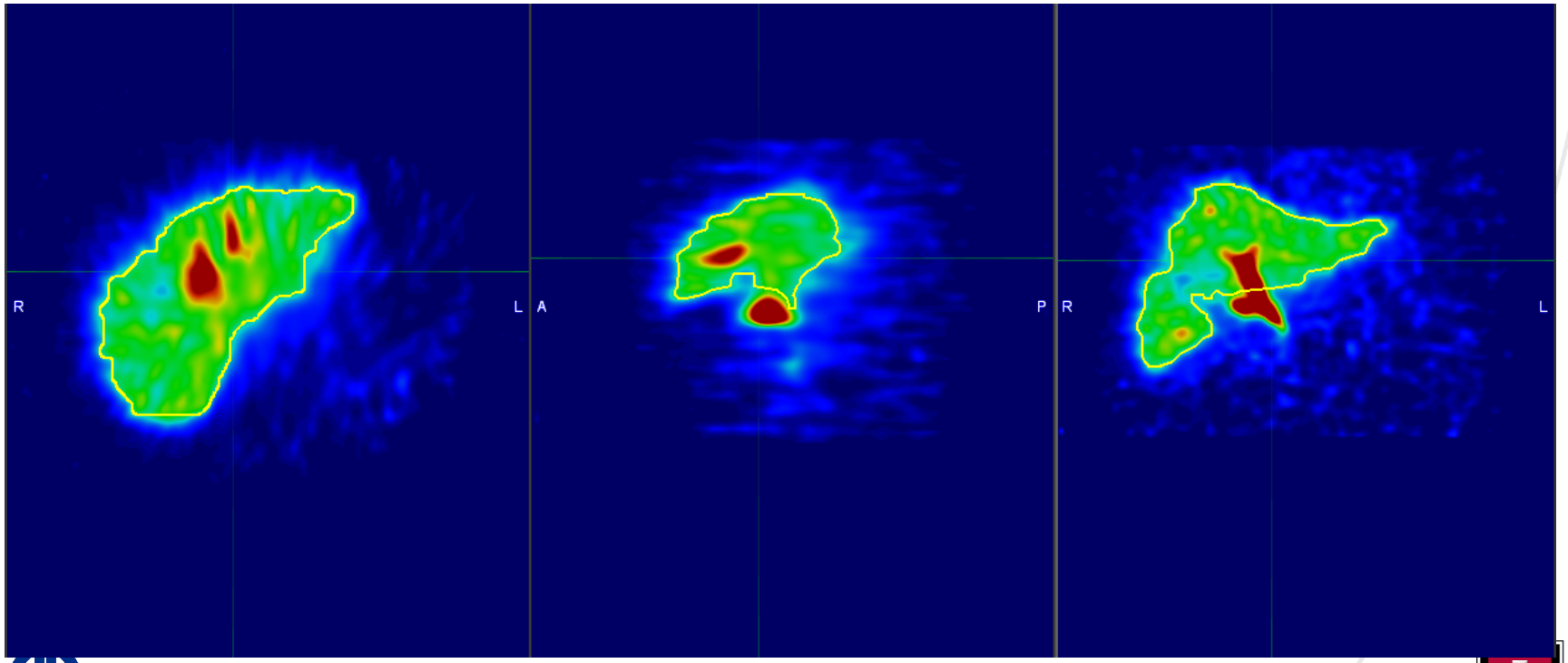
* Erdogan et al, Liver International 2004, 24, 117-123

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 $= \frac{Rate\ of\ liver\ uptatke\ between\ 150-300\ s}{Body\ surface\ area}$



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* =

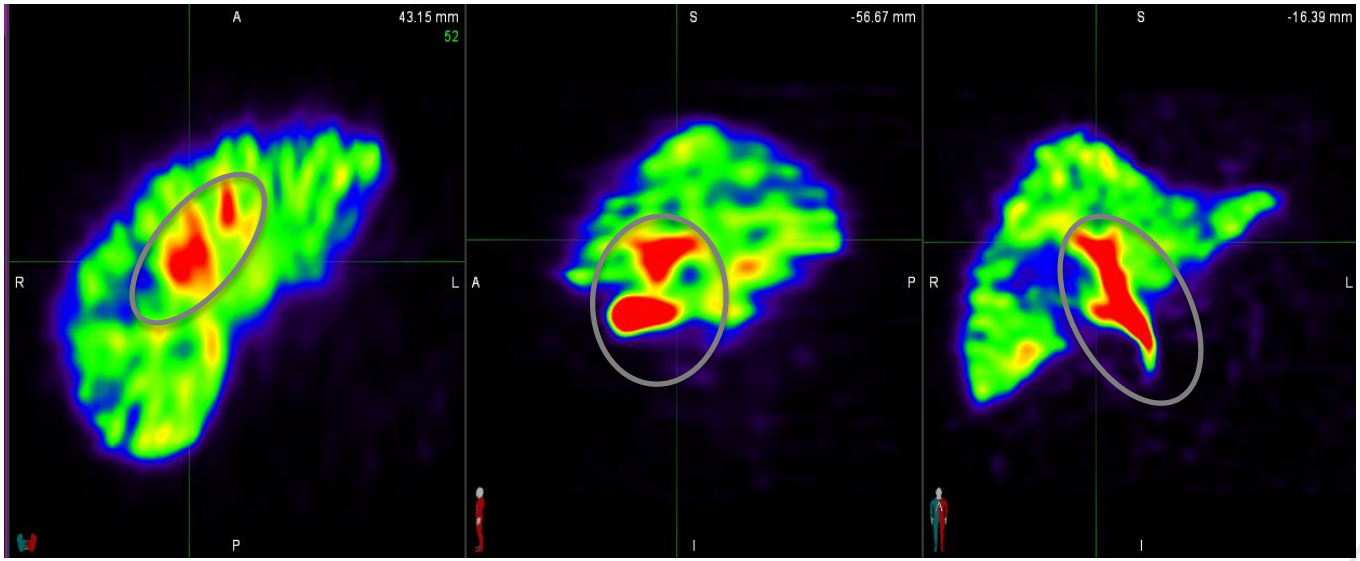
$$\frac{Rate\ of\ liver\ uptatke\ between\ 150{-}300\ s}{Body\ surface\ area}$$

- Unit - %/min/m^2

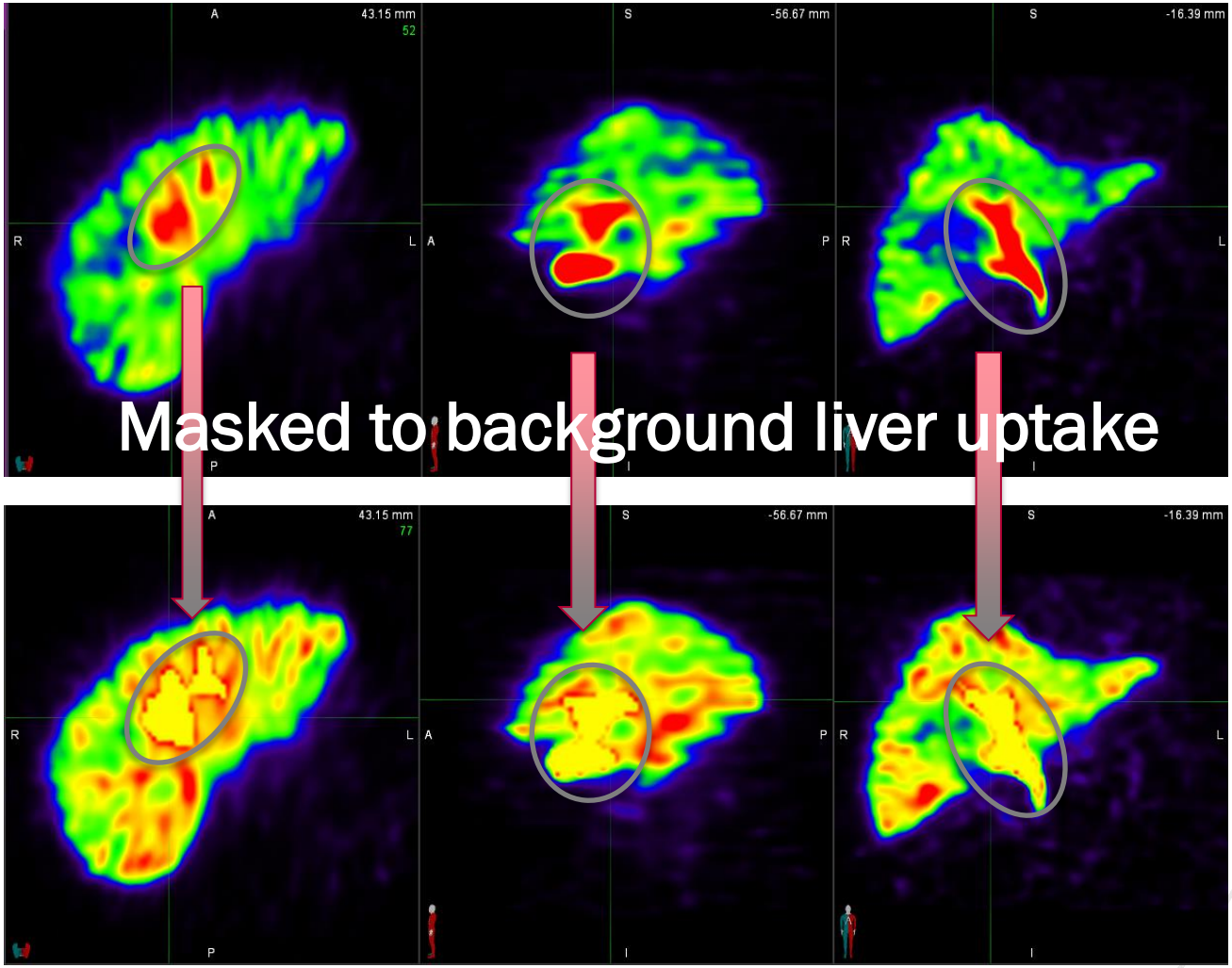
* Long et al, Practical Radiation Oncology (2018) 8, 429-436

High Value in Bile Duct

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

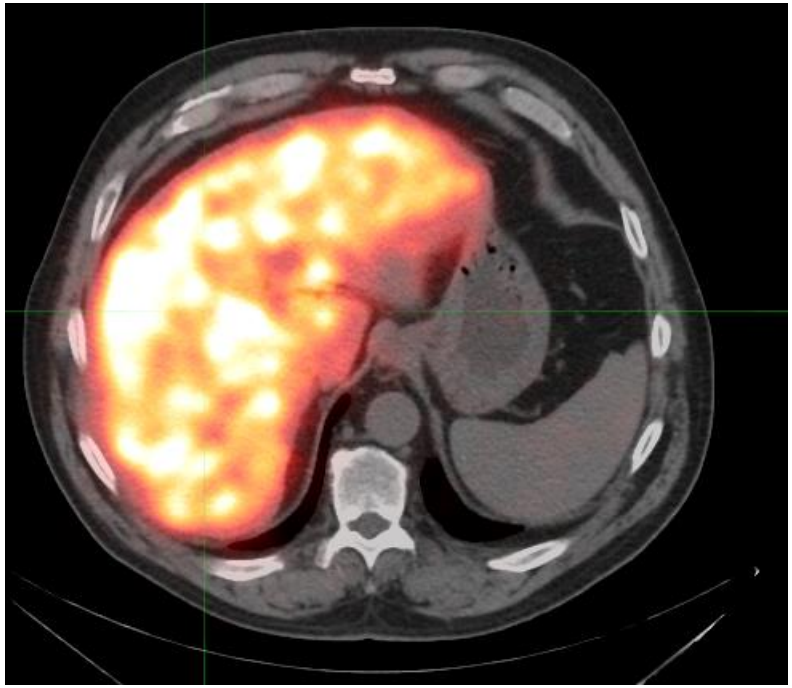


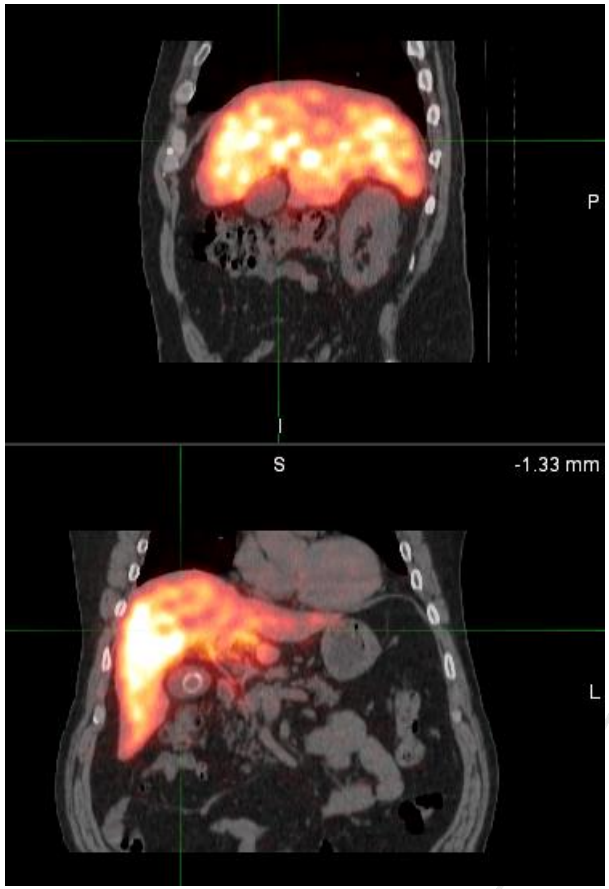
Bile Duct Mask



Contouring the Functional Areas

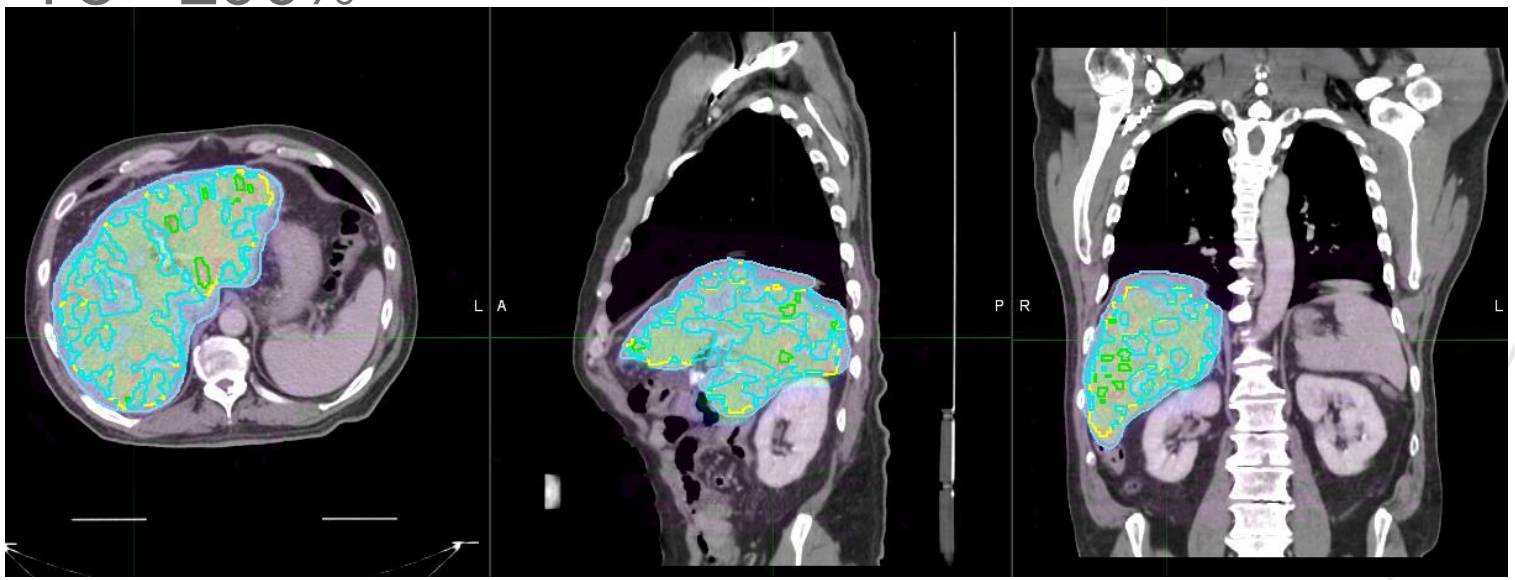
- HIDA scan was fused to the planning computed tomography with contours generated from percent of maximum





Contouring the Functional Areas

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



FLIGHT Planning

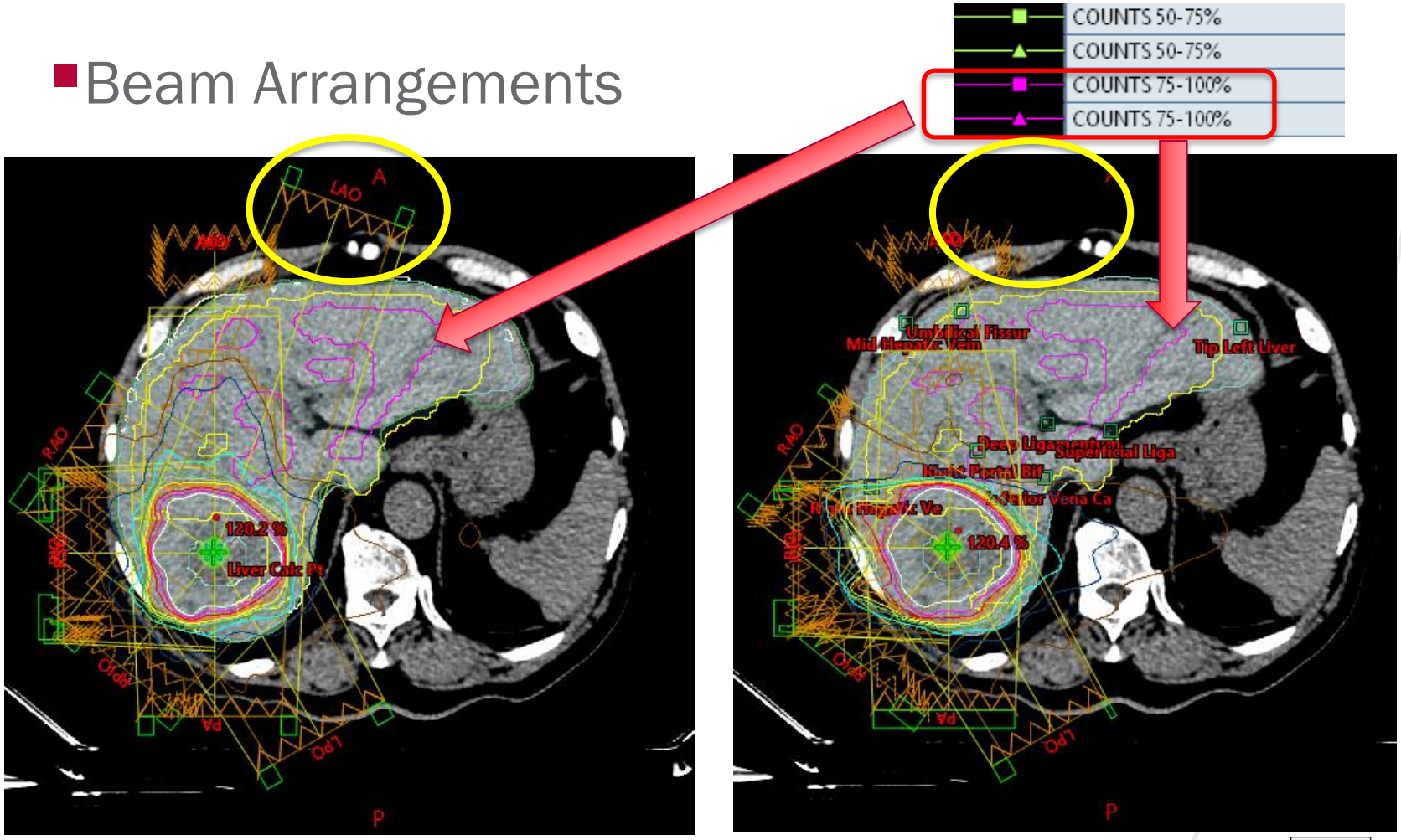
- Functional liver image guided hepatic therapy planning (FLIGHT)
- Primary goal of FLIGHT planning was to maximize the functional residual capacity (FRC) of the liver.
- Minimize dose to the highest functioning liver (HIDA uptake 50%- 100% max)
- To preferentially distribute dose through the regions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

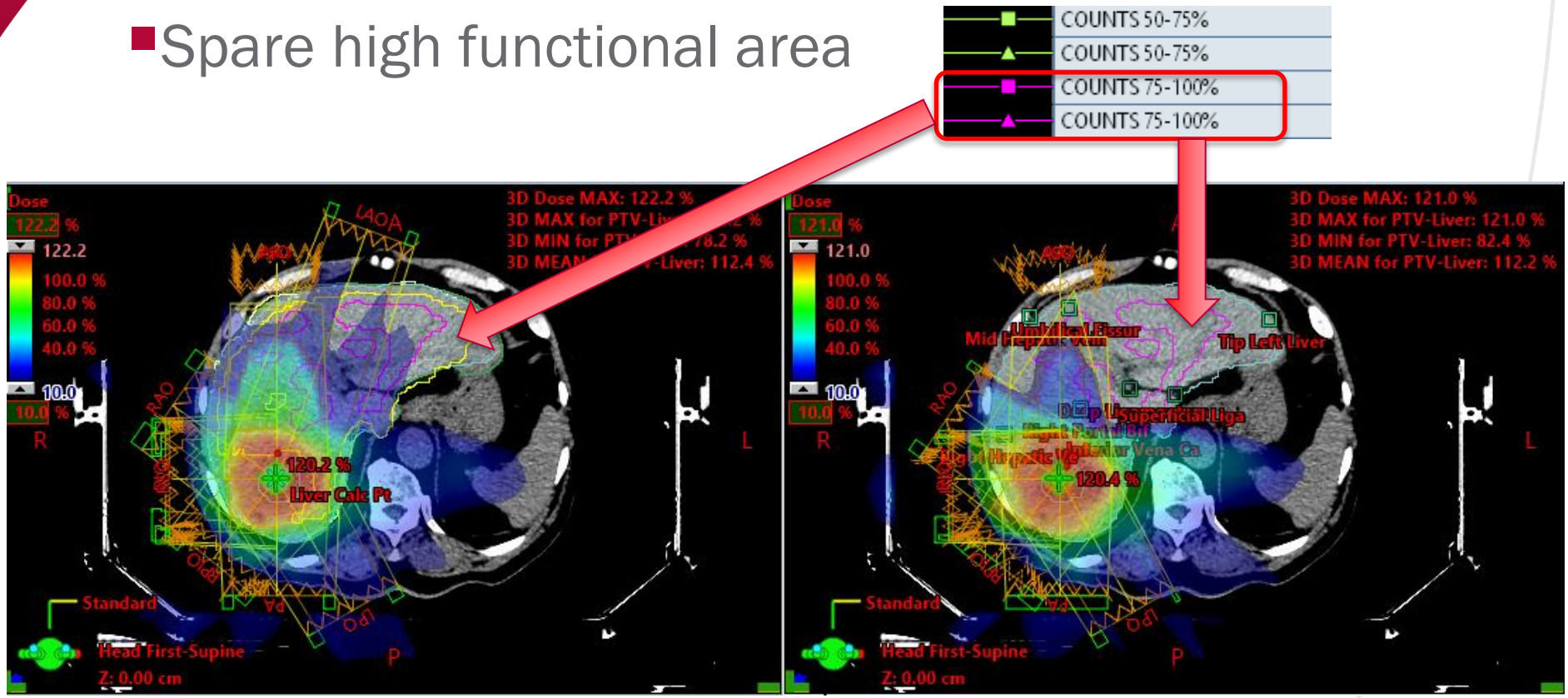
Optimization

- Tighter constraints on higher functional area

☑ COUNTS 25-50%		Volume [cc]:	602	Points:	20052	Resolution [mm]:	3.00
	Upper	Volume [%]:	49.5	Dose [cGy]:	1035.0	Priority:	50
	Upper		41.5		1836.6		50
	Upper		33.1		2903.1		50
	Upper		23.7		3762.1		50
☑ COUNTS 50-75%		Volume [cc]:	1008	Points:	33588	Resolution [mm]:	3.00
	Upper	Volume [%]:	13.1	Dose [cGy]:	643.9	Priority:	60
	Upper		3.5		1474.4		60
	Upper		32.5		190.6		60
	Upper		0.8		2461.3		60
	Upper		51.5		18.4		60
☐ **COUNTS 50-100%**		**Volume [cc]:**	**1233**	**Points:**	**41099**	**Resolution [mm]:**	**3.00**
☑ COUNTS 75-100%		Volume [cc]:	229	Points:	7625	Resolution [mm]:	3.00
	Upper	Volume [%]:	38.3	Dose [cGy]:	41.3	Priority:	50
	Upper		21.5		86.8		50
	Upper		7.0		306.1		50
	Upper		1.4		776.0		50
	Upper		0.5		1320.4		50

FLIGHT vs Standard SBRT

- Spare high functional area

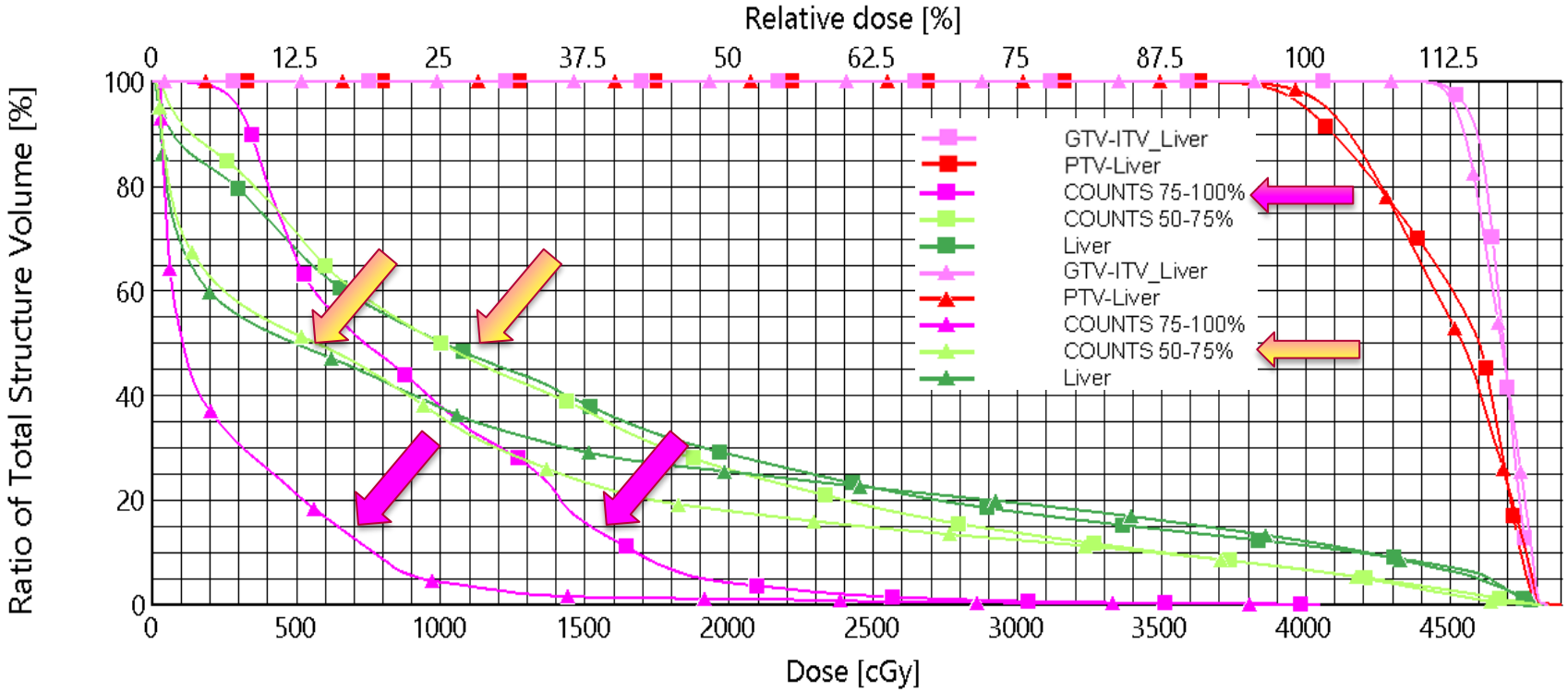


Standard SBRT

FLIGHT SBRT

FLIGHT vs Standard SBRT - DVHs

- Standard SBRT
- FLIGHT SBRT



Functional DVH (fDVH)

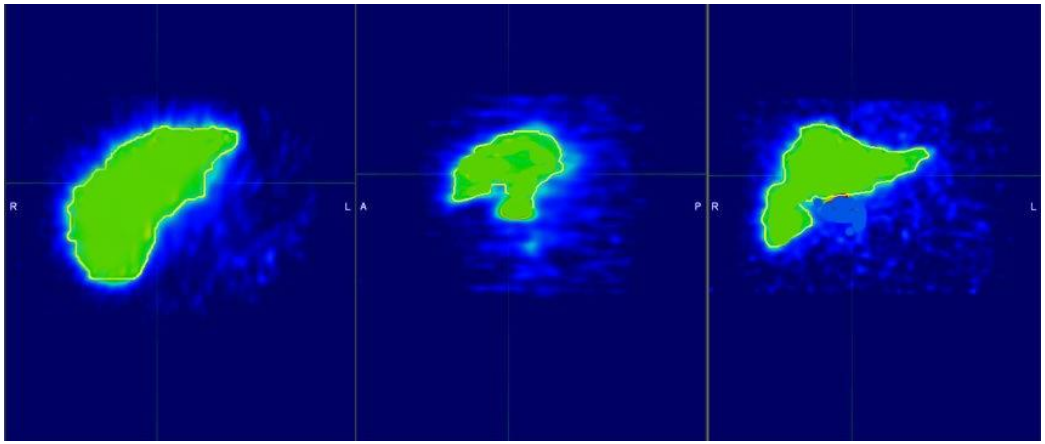
- Traditional DVH does not consider the functional competence of different regions.* (Duke University)
- The functional dose–volume histogram is a variation of the dose–volume histogram (DVH), which incorporates the non-uniform distribution of functional subunits into the dose–volume consideration.**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

* Marks et al, I. J. Radiation Oncology Biol. Phys. 1995, V33, No1, 66-75

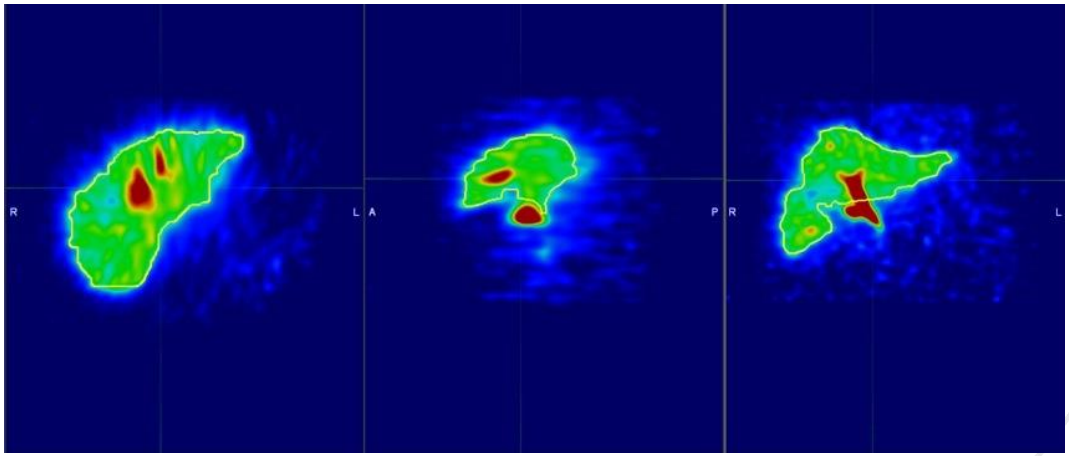
** Lu et al, Phys. Med. Biol. 42 (1997) 345–356

DVH vs fDVH

- DVH (assume uniform function distribution)



- fDVH (Nonuniform function distribution)



Functional DVH

- $fDVH(D_0) =$ *number of functional units receiving at least the dose* D_0 $*$ / *total number of functional units*

$$\mathrm{fDVH}(D_0) = \frac{\int_{V_0} \mathrm{d}\boldsymbol{r}\, f(\boldsymbol{r})\Theta(D(\boldsymbol{r}) - D_0)}{\int_{V_0} \mathrm{d}\boldsymbol{r}\, f(\boldsymbol{r})}$$

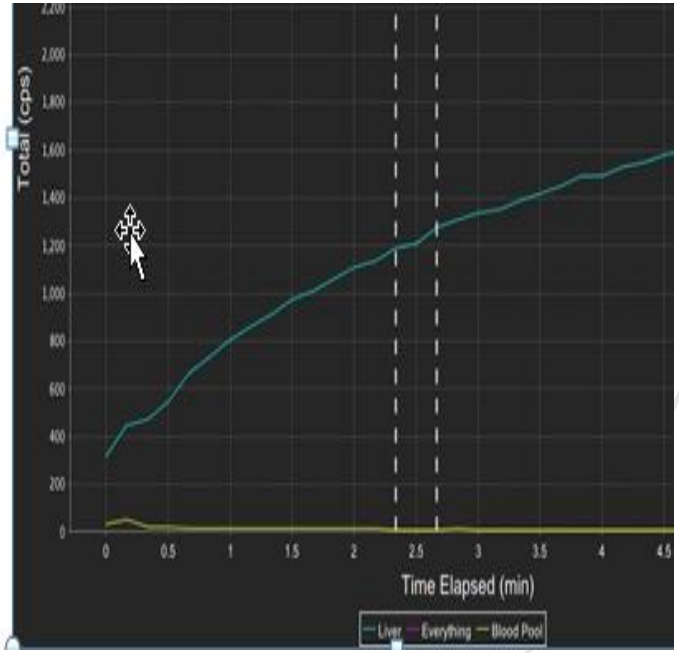
$\Theta(D(\boldsymbol{r}) - D_0)$ *is the step function which is 1 when* $D(r) > D_0$ *and 0 when* $D(r) < D_0$

* Lu et al, Phys. Med. Biol. 42 (1997) 345–356

Absolute fDVH

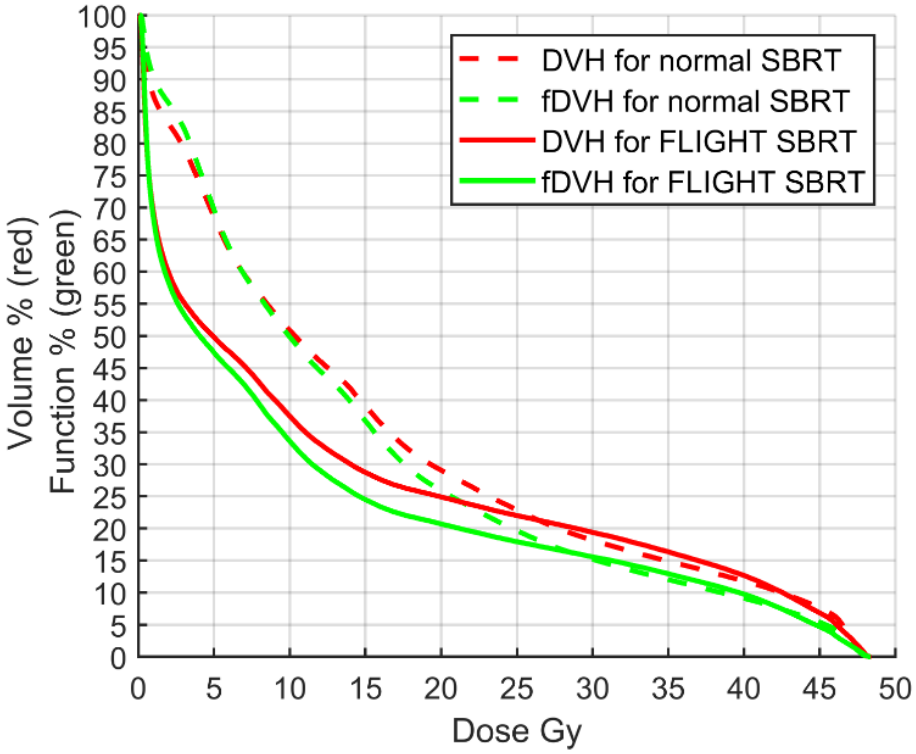
- Absolute fDVH(D_0) = % fDVH(D_0) × Global HIDA Value
- Global HIDA Value =

$$\frac{Rate\ of\ liver\ uptatke\ between\ 150{-}300\ s}{Body\ surface\ area}$$

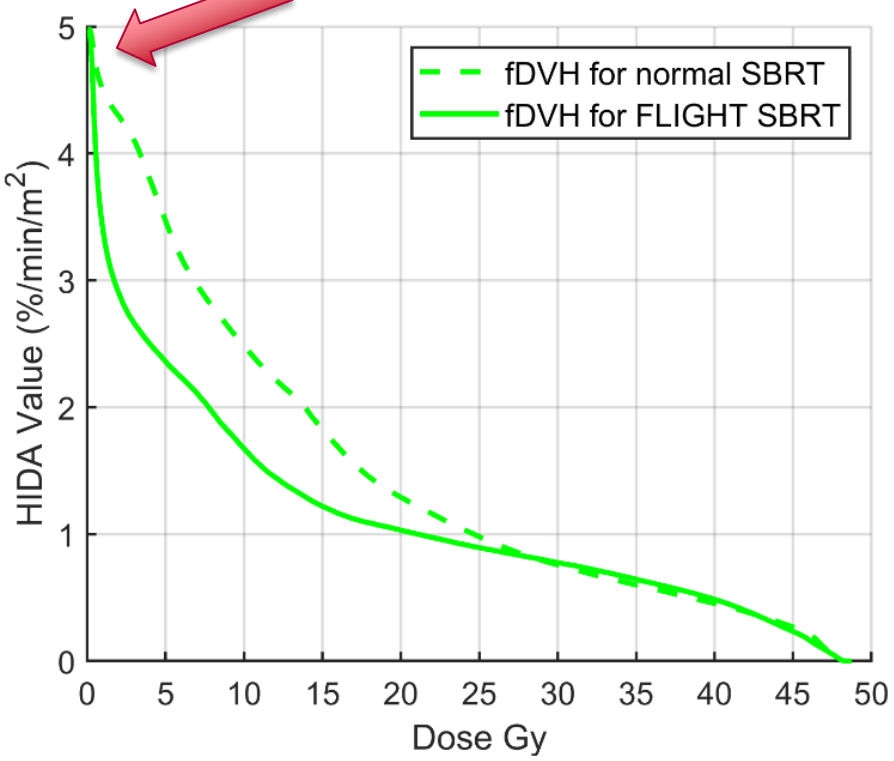


DVH and fDVH for normal vs FLIGHT SBRT

- % fDVH
- Absolute fDVH



Global HIDA Value:
4.98%/min/m2



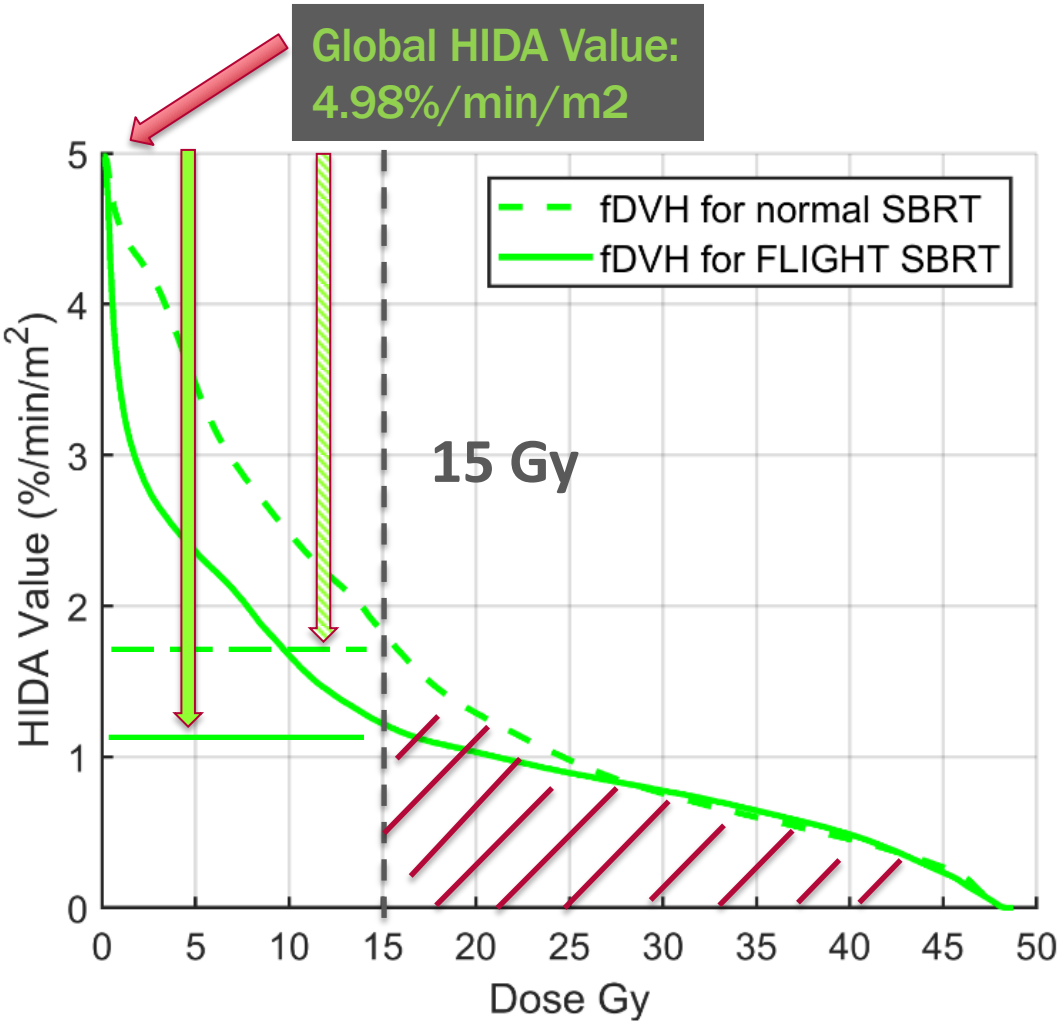
FRC_{15} HIDA

- Functional residual capacity < 15 Gy
- FRC_{15} HIDA =(%counts <15 Gy) × (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, 17Gy (University of Michigan)***

* Long et al, Practical Radiation Oncology (2018) 8, 429-436
** Lasley et al, Practical Radiation Oncology (2015) 5, e443-e449
*** Cao et al, Int J Radiat Oncol Biol Phys 2013;85:258-263

FRC_{15} HIDA for normal vs FLIGHT SBRT

- Functional residual capacity < 15Gy
- —— FLIGHT SBRT
- - - - normal SBRT
- FRC_{15}HIDA for FLIGHT is 3.76
- FRC_{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.*
- $EUD = \left(\sum_{i=1}^{N} v_i D_i^a / \sum_{i=1}^{N} v_i \right)^{1/a}$ **
- *a was calcuated using* $TD_{5/5}(1) = TD_{5/5}(v) v^{1/a}$

* Niemierko, Medical Physics 24, 103, 1997

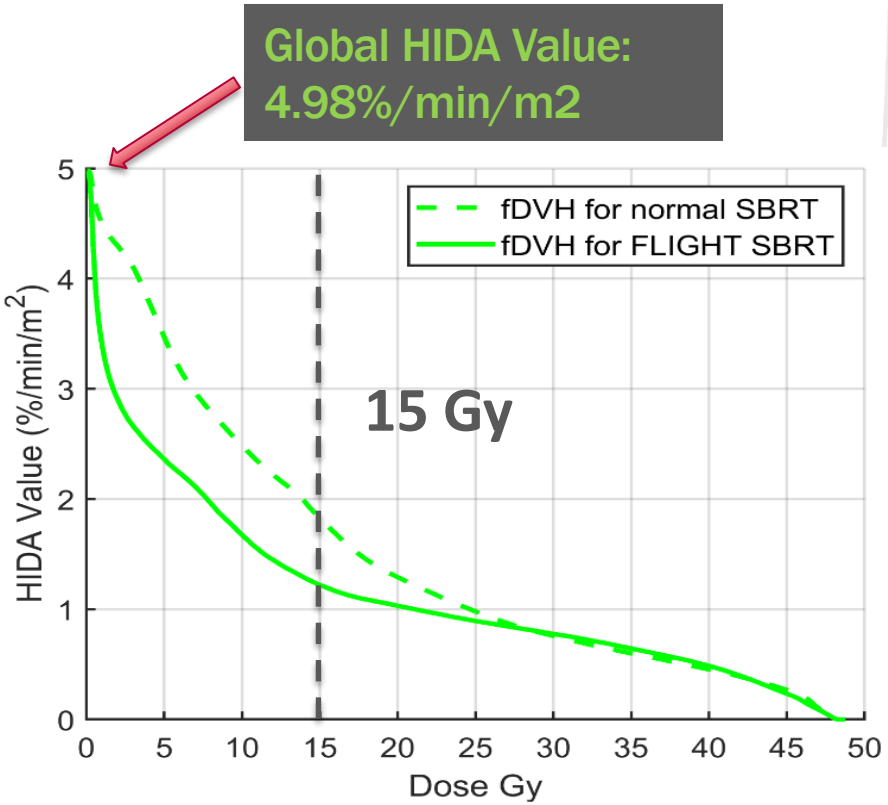
** Miften, Phys. Med. Biol. 49 (2004) 1711–1721

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
- $FEUD = \left(\sum_{i=1}^{N} f_i D_i^a / \sum_{i=1}^{N} f_i \right)^{1/a}$

* Miften, Phys. Med. Biol. 49 (2004) 1711–1721

FLIGHT vs normal SBRT



	Standard	FLIGHT	Relative Improvement
$FRC_{15}HIDA$ (%/min/m²)	3.15	3.76	19.40%
Mean Liver Dose (Gy)	15.11	12.55	16.90%
EUD	22.02	21.26	3.40%
FEUD	20.59	19.33	6.10%

FLIGHT vs normal SBRT - statistics

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

	Standard (n = 17)	FLIGHT (n = 17)	Mean relative improvement (Range)	*P*-value
Mean FRC_{15} HIDA (%/min/m^2)	2.48	2.63	5.3% (1.2-20.2%)	.012
Mean liver dose (Gy)	9.07	7.89	14.7% (0.9-33.6%)	< .001
Mean EUD	16.14	15.15	6.2% (–0.2 to 16.6%)	< .001
Mean FEUD	16.14	14.89	7.9% (0.04-18.7%)	< .001
Conformality index	1.03	1.01		.348
Gradient index	3.75	3.55		.087

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

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Questions