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MARLENE AND STEWART GREENBERG  
COMPREHENSIVE CANCER CENTER

## Theranostic Imaging and Functional Image-Guided Head-And-Neck Radiation Therapy

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### Squamous cell carcinoma of the head and neck

Estimated New Cases in 2019	53,000
% of All New Cancer Cases	3.0%
Estimated Deaths in 2019	10,860
% of All Cancer Deaths	1.8%

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### From discrete volumes to 3D maps

~1980      ~1990      2010+  
CTV2  
<sup>61</sup>Cu-ATSM hypoxia scan - UW

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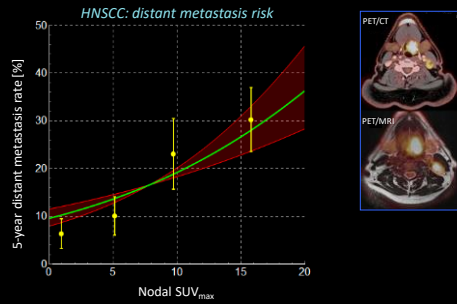
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### Imaging: spatial AND biological information



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### Dose painting & personalized RT prescription

#### Personalized prescription

- varying the 4D dose prescription between patients according to some (imaging?) biomarker
  - Risk based (*predictive*)
  - Response based (*adaptive*)



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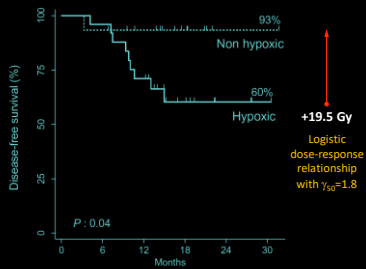
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### FAZA PET/CT: DAHANCA 24



Pts at risk:

Non hypoxic:	15	14	11	6	1	1
Hypoxic:	25	24	17	8	3	1

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Mortensen et al. *R&O* 105; 14 (2012)

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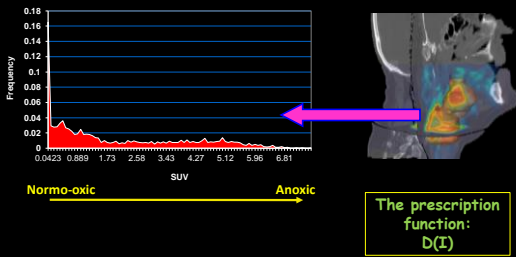
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### Dose-painting by numbers



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Bentzen *Lancet Oncology* 6: 112 (2005)

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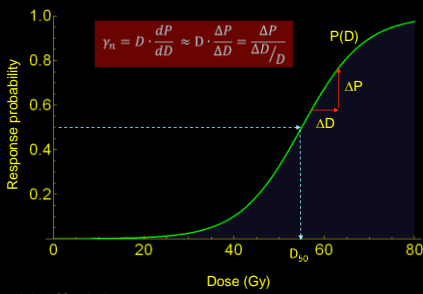
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### The normalized dose-response gradient



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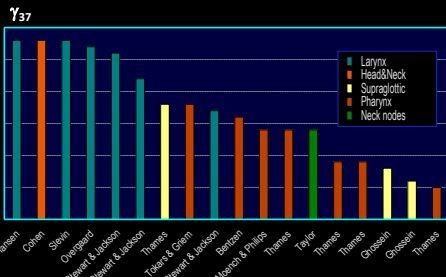
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### Steepness of dose-response curves for HNSCC



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Bentzen *R&O* 32: 1 (1994)

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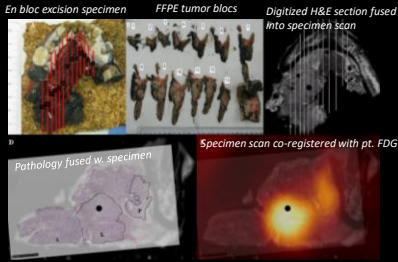
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## Functional Imaging of Heterogeneity in Head and Neck Tumors (FIGHTT)



- 28 patients w. 31 lesions
- 6 random biopsies from each
- In vivo and ex vivo scans + pathology
- Large intra-tumor variability
- Significant but weak correlations between FDG and #viable tumor cells and CAIX

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 PI: Jacob Rasmussen, MD – UH Copenhagen /SMB 7/19

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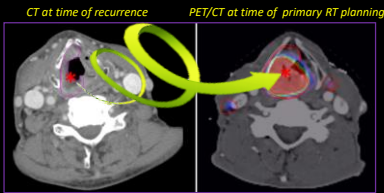
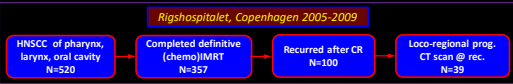
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## Focal origin of recurrence



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 AK Due et al. *Strahlenther Onkol* 188: 671 (2012) /SMB 7/19

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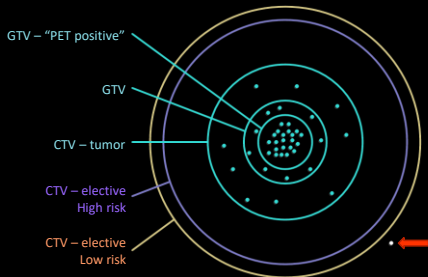
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## Pattern of recurrence



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 AK Due et al. *R&O* 111: 360 (2014) /SMB 7/19

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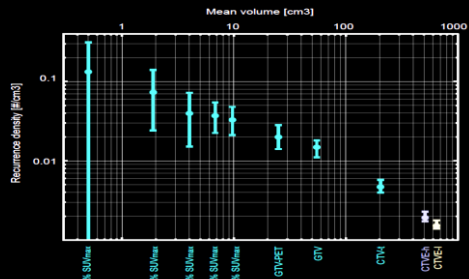
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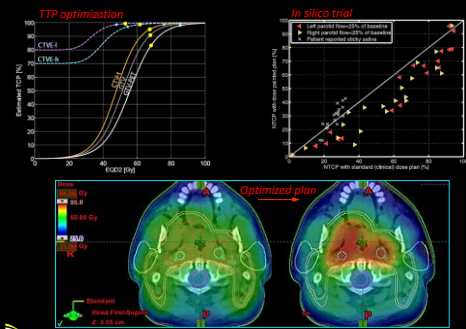
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## Recurrence density after RT for HNSCC



## Data-driven dose redistribution



## The CONTRAST Phase I dose-escalation trial

**CONTRAST: CONventional vs. Tumor Recurrence Adapted Specification of Target dose**

Population: locally advanced HNSCC treated with (chemo)radiation therapy at Rigshospitalet in Copenhagen

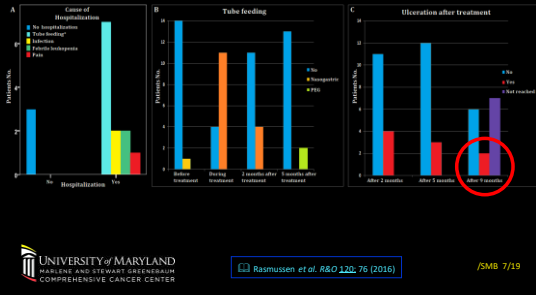
**DESIGN:**

```
graph TD
    A[Accrue 15 patients] --> B[5/15 toxic events G4+]
    A --> C[1/15 toxic events G4+]
    A --> D[2+ toxic events G4+]
    B --> E[Escalate dose]
    C --> F[Accrue 15 patients]
    D --> G[Stop]
    E --> H[1/10 or 2/10 toxic events G4+]
    E --> I[3+ toxic events G4+]
    H --> J[Escalate dose]
    I --> K[Stop]
```

Dose level	Target doses [EQD2 (Gy)]					Estimated TCP (%) w/o persist. disease	All cases	Total sample size in phase III
	CTV <sup>e-h</sup>	CTV <sup>e-l</sup>	CTV	GTV	GTV+PET			
Current	52.9	61.6	68	68	68	70	59.5	-
Step 1	50.8	58.8	70	74	82	84.3	71.6	672
Step 2	49.6	57.5	70	75	85	87	74	470



The CONTRAST Phase I dose-escalation trial




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CONTRAST Phase I dose-escalation trial

Penetration of soft palate 8 months after RT

Same patient 9 months after RT – after attempted surgical reconstruction

Dose Gy scale: 35 to 85

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Particle Swarm Optimization – breast case

**CLINICAL**

- PSO – an algorithm for finding maxima on complex surfaces
- All bioeffect models evidence based.

**PSO**

Examples of models:

$$DFS_{CTVx} = DFS_{baseline}^{HR_{CTVx}}$$

$$= 0.363^A \left( 1 - 0.47 \frac{CTVx}{50 Gy} \right)$$

$$Risk_x = w_x * DFS * hr_{excess,age}^{80\text{ yr}} * h_{gen.pop,x}(a,sex) * (S_{gen}(a,sex)) da$$


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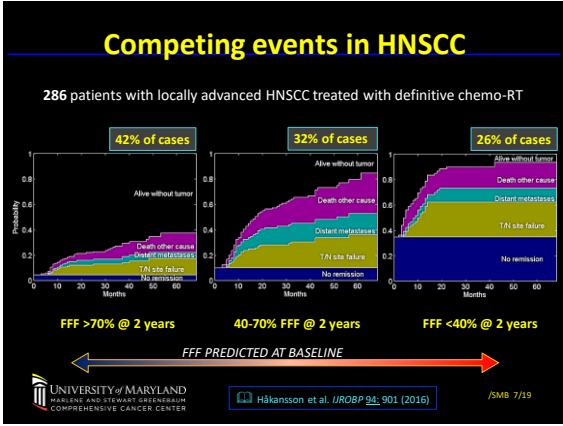
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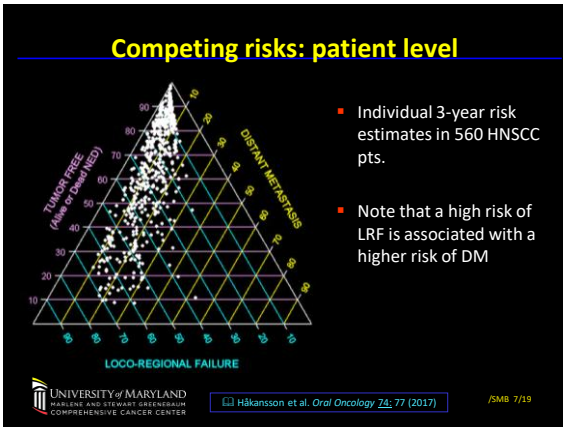
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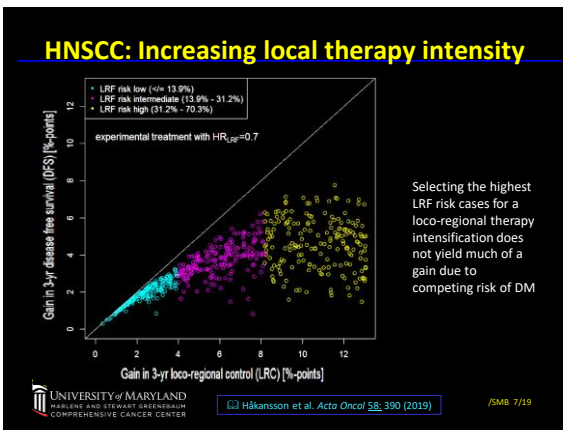
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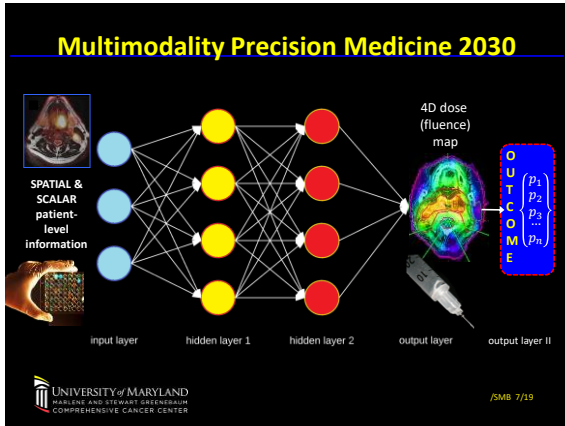
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