


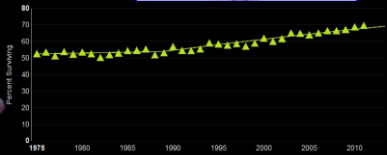

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Theranostic Imaging and Functional Image-Guided Head-And-Neck Radiation Therapy

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Squamous cell carcinoma of the head and neck

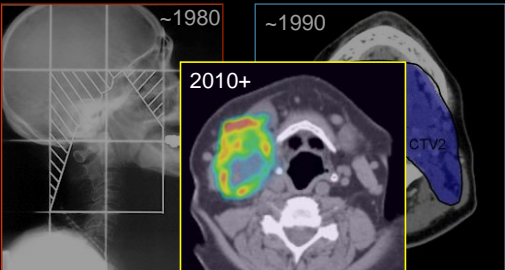
Estimated New Cases in 2019	53,000
% of All New Cancer Cases	3.0%
Estimated Deaths in 2019	10,860
% of All Cancer Deaths	1.8%



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From discrete volumes to 3D maps



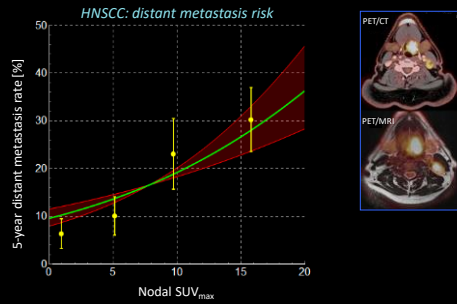
~1980 ~1990 2010+ CTV2

⁶¹Cu-ATSM hypoxia scan - UW

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Imaging: spatial AND biological information



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Dose painting & personalized RT prescription

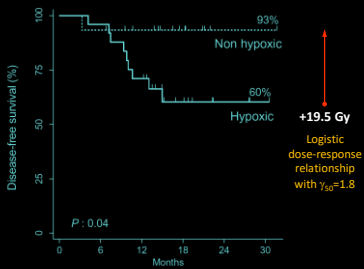
- Personalized prescription
 - varying the 4D dose prescription between patients according to some (imaging?) biomarker
 - Risk based (*predictive*)
 - Response based (*adaptive*)



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FAZA PET/CT: DAHANCA 24



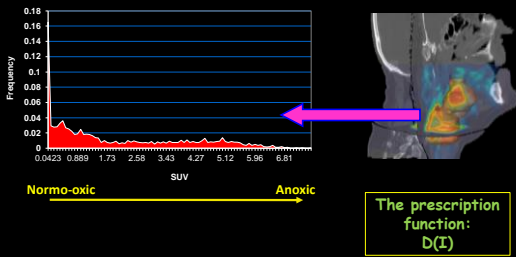
Pts. at risk:	0	6	12	18	24	30
Non hypoxic:	15	14	11	6	1	1
Hypoxic:	25	24	17	8	3	1

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

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Dose-painting by numbers

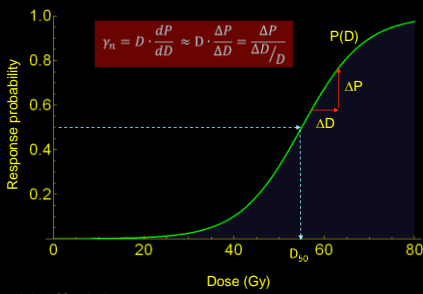


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Bentzen *Lancet Oncology* 6: 112 (2005)

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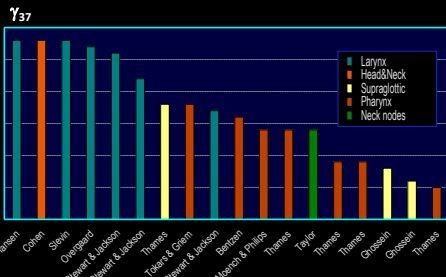
The normalized dose-response gradient



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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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Functional Imaging of Heterogeneity in Head and neck Tumors (FIGHHT)

- En bloc excision specimen
- FPPE tumor blocs
- Digitized H&E section fused into specimen scan
- Pathology fused w. specimen
- Specimen scan co-registered with pt. FDG

- 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

Focal origin of recurrence

Rigshospitalet, Copenhagen 2005-2009

HNSCC of pharynx, larynx, oral cavity N=520

Completed definitive (chemo)IMRT N=357

Recurred after CR N=100

Loco-regional prog. CT scan @ rec. N=39

CT at time of recurrence

PET/CT at time of primary RT planning

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

Pattern of recurrence

GTV – “PET positive”

GTV

CTV – tumor

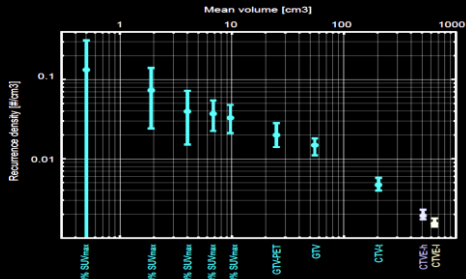
CTV – elective High risk

CTV – elective Low risk

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

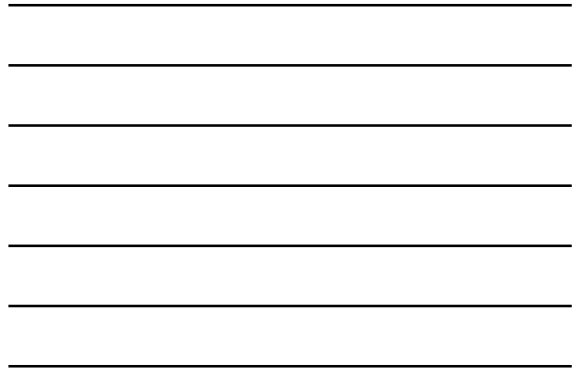
Recurrence density after RT for HNSCC



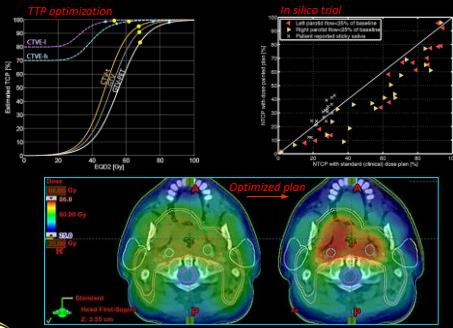
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Ax Due et al. *RRO* 111, 360 (2014)

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Data-driven dose redistribution



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IR Vogelius et al. *Med Phys* 40, 081717 (2013)

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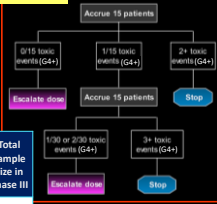
The CONTRAST Phase I dose-escalation trial



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

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

DESIGN:



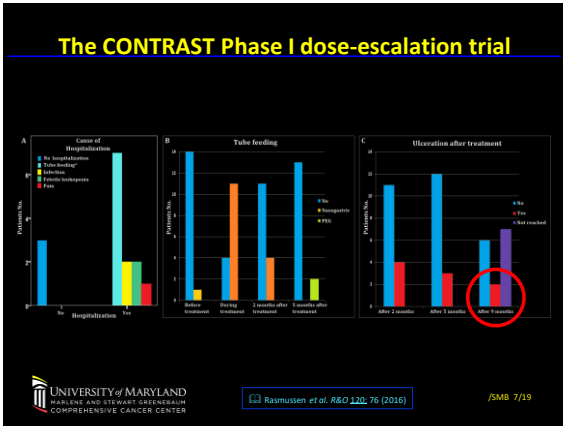
Dose level	Target doses [EQD2 (Gy)]					Estimated TCP [%]	Total sample size in phase III
	CTV _{eH}	CTV _{eL}	CTV	GTV	GTV-PET		
Current	52.9	61.6	68	68	68	70	59.5
Step 1	50.8	58.8	70	74	82	84.3	71.6
Step 2	49.6	57.5	70	75	85	87	74

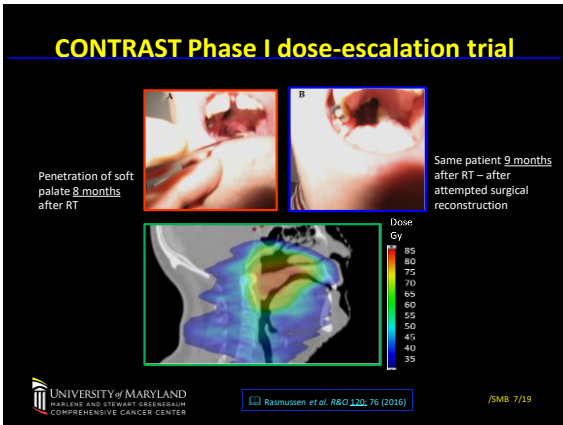
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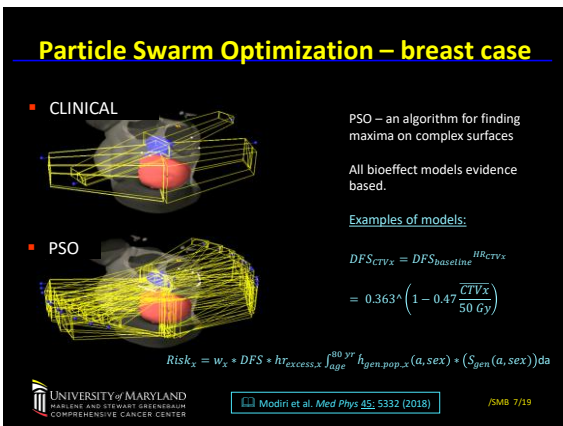
Rasmussen et al. *RRO* 120, 76 (2016)

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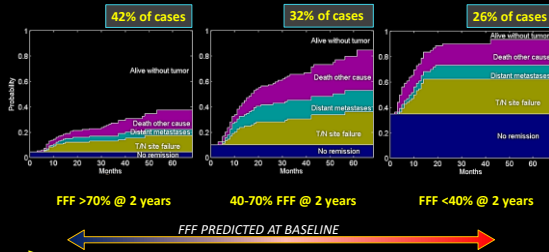






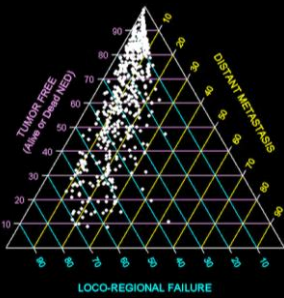
Competing events in HNSCC

286 patients with locally advanced HNSCC treated with definitive chemo-RT



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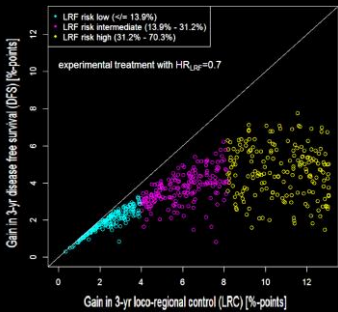
Competing risks: patient level



- Individual 3-year risk estimates in 560 HNSCC pts.
- Note that a high risk of LRF is associated with a higher risk of DM

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HNSCC: Increasing local therapy intensity



Selecting the highest LRF risk cases for a loco-regional therapy intensification does not yield much of a gain due to competing risk of DM

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