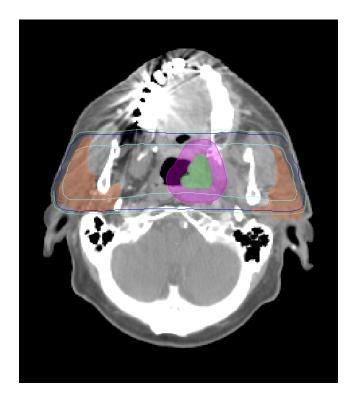


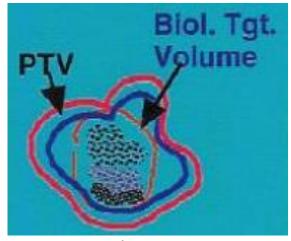




### Background

- Radiotherapy is a balance between tumor and side effects
- Traditionally radiotherapy has been administered with a homogeneous dose to the tumor
- The dose painting hypothesis is to increase the dose to the most aggressive sub volumes of the tumor as depicted on biological imaging – and thereby improve local control – without increasing the level of side effects





Ling et al IJROBP 2000









#### Molecular Imaging-Guided Radiotherapy for the Treatment of Head-and-Neck Squamous Cell Carcinoma: Does it Fulfill the Promises?



Vincent Grégoire, MD, PhD,\*,† Daniela Thorwarth, PhD,‡ and John Aldo Lee, Eng, PhD†

2017

... in the coming years, one may expect to position the dose painting approach in the armamentarium for the treatment of patients with head-and-neck squamous cell carcinoma.





#### MR linac

# The ViewRay<sup>TM</sup> System

- Washington University in Saint Louis
- UW Madison



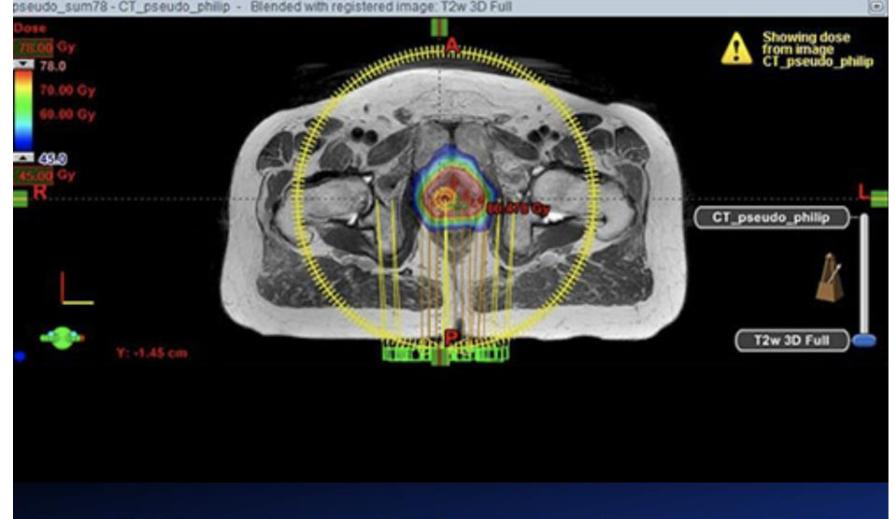


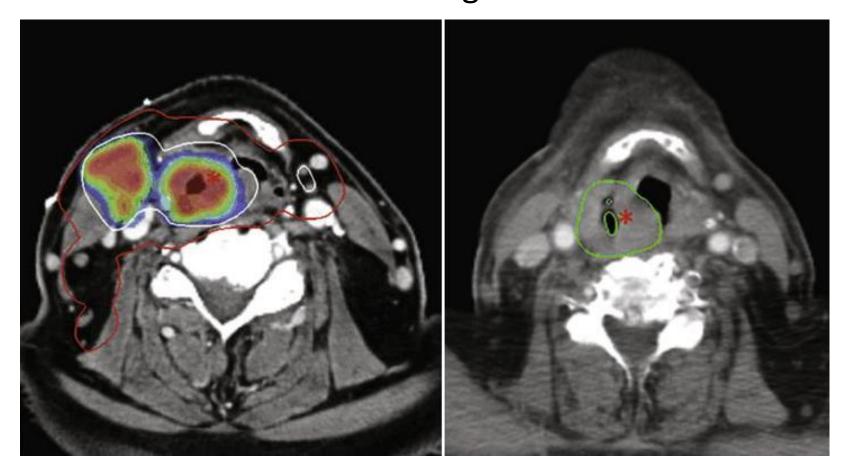
Image 2: RT dose plan based on MR-only simulation, overlay on T2W 3D imaging

Image courtesy of Docrates Cancer Center, Helsinki, Finland





# Dose painting rationale: Recurrences often localised in the 18F-FDG-PET avid volume and high RT dose volume

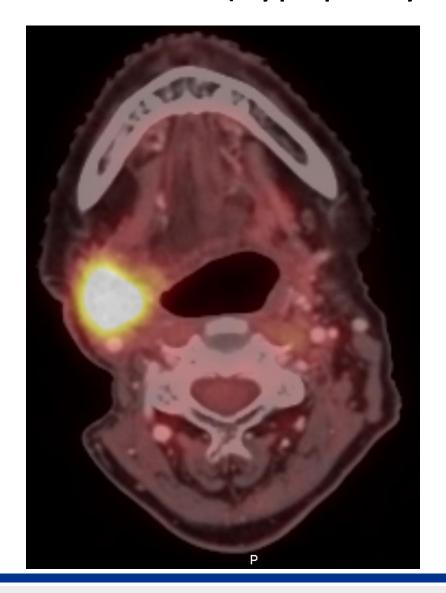


Hypopharyngeal cancer. Recurrence on CT (right) at the location of the primary tumor, 7 months after primary radiochemotherapy; Due et al R&O -14.



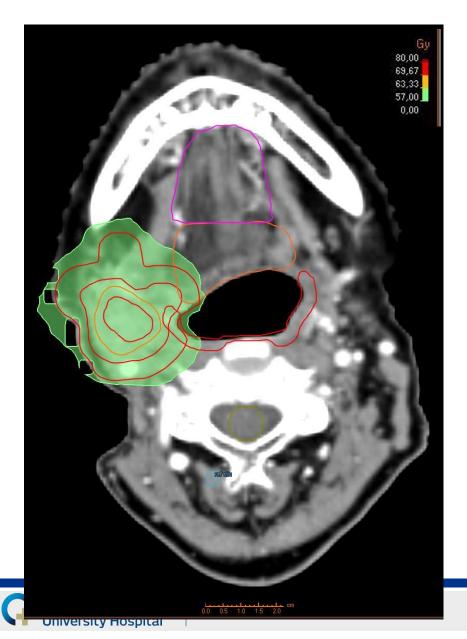


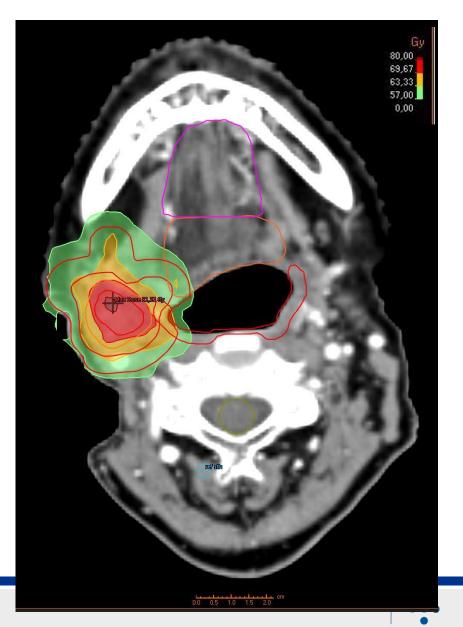
#### Lymph node recurrence (hypopharyngeal cancer)

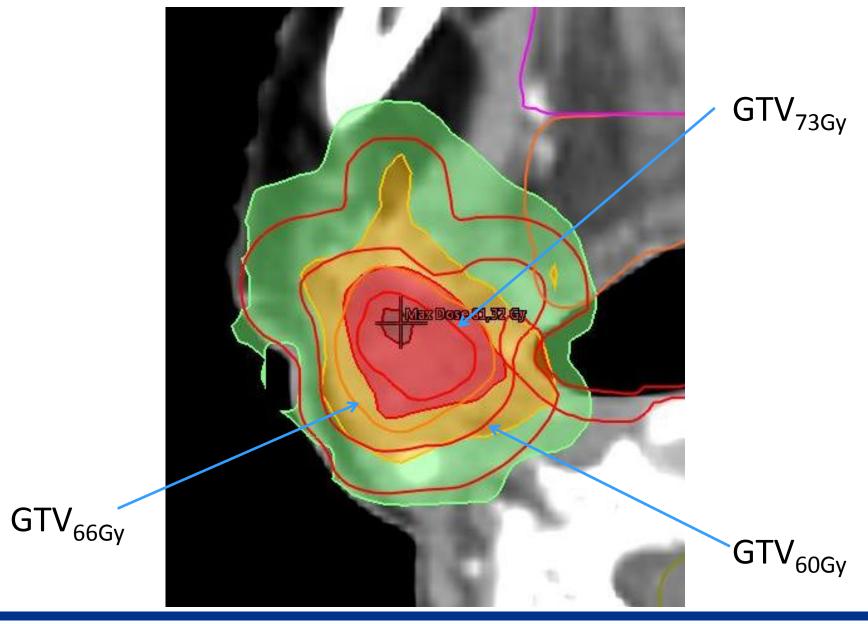




## Conventional vs dose painting



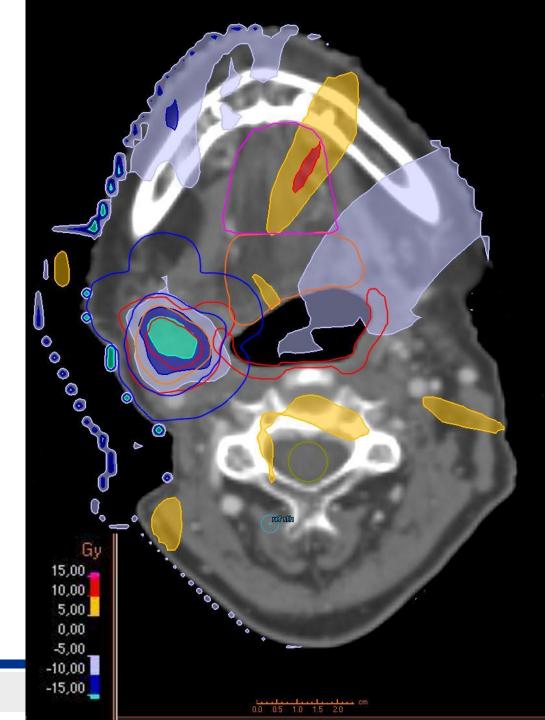




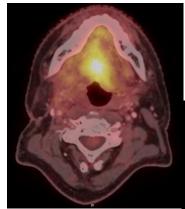




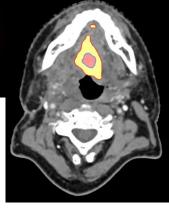
Subtraction between dose painting and conventional RT (red favours DP)

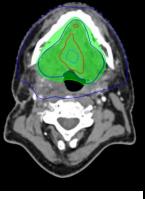


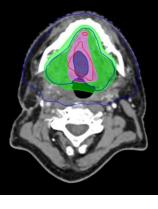


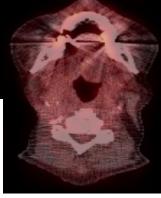


#### Dose painting









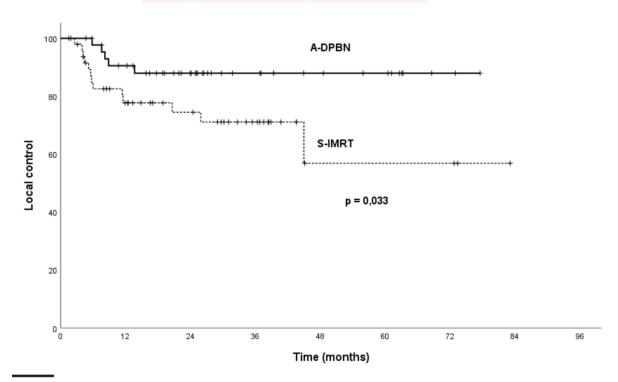




#### **ESTRO 2019**

#### **Local control**

	A-DPBN	S-IMRT
1Y	91%	78%
2Y	88%	<b>75</b> %







#### ORIGINAL ARTICLE



# Late mucosal ulcers in dose-escalated adaptive dose-painting treatments for head-and-neck cancer

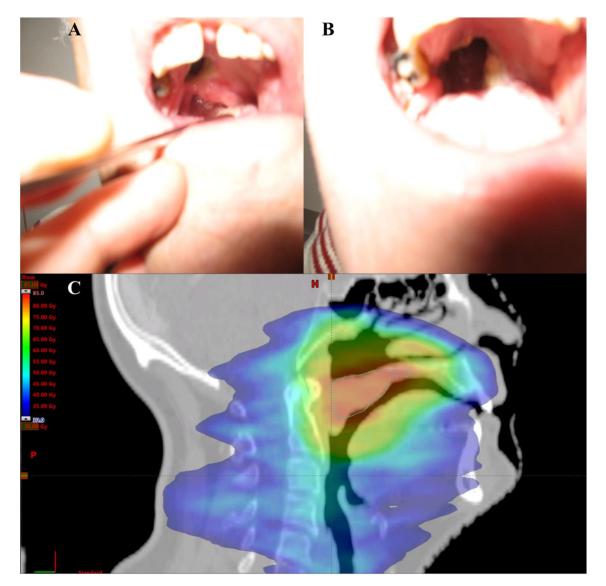
Luiza Ana Maria Olteanu<sup>a</sup>, Fréderic Duprez<sup>a</sup>, Wilfried De Neve<sup>a,b</sup>, Dieter Berwouts<sup>c</sup>, Tom Vercauteren<sup>a</sup>, Wouter Bauters<sup>d</sup>, Philippe Deron<sup>e</sup>, Wouter Huvenne<sup>e</sup>, Katrien Bonte<sup>e</sup>, Ingeborg Goethals<sup>c</sup>, Julie Schatteman<sup>a</sup> and Werner De Gersem<sup>b</sup>

Results: From 39 studied patients, nine developed late grade 4 mucosal ulcers. The continuation to either smoke or drink alcohol after therapy was the factor that showed a strong (eight out of nine patients) association with the occurrence of grade 4 ulcers. Six of the patients who continued to smoke or/and drink had D<sub>1.75cc</sub> and NID2<sub>1.75cc</sub> above 84Gy and 95.5Gy, respectively. Seven of the patients with grade 4 had the dose levels above these thresholds, but even if the  $D_{1.75cc}$ threshold was significant in the prediction of late grade 4 ulcers, it could not be considered as the only contributing factor. Conclusions: The search for patterns provided strong reasons to apply a dosimetrical threshold for the peak-dose volume of 1.75 cm3 as a preventive measure for late grade 4 mucosal ulcers. Also, patients that continue to smoke or drink alcohol after therapy have increased risk to develop late mucosal ulcers.





#### Skade i bløte gane etter dose painting



Rasmussen et al, Radiotherapy & oncology 2016



# Dose painting trial at Oslo University Hospital

- Part of a larger study, RIOT- Re-Irradiation or Other Treatment of patients with Head and Neck cancer unsuited for radical radiotherapy, Evaluation with Patient Reported Outcome
- Main study: Inclusion June -15 to May -19: 151(?) pts
- Sub study IIb: RIDPAINT Dose-painting feasibility trial. N = 10.





#### RIDPAINT - purpose

#### **Primary Outcome Measure:**

 To test the <u>feasibility</u> (success rate and workload) of FDG-PET guided dose painting for patients with recurrent or second primary head and neck cancer.

#### Secondary Outcome Measures:

- Evaluate acute toxicity
- Evaluate tumour response (at 3 months after RT) with PET-CT according to RECIST and SUV analyses.
- Evaluate time to (clinical) progression.





#### RIDPAINT – inclusion criteria

- Referred for reirradiation of the head & neck (recurrence or second primary)
- Inoperable disease
- Histology: Squamous cell carcinoma
- < grade 3 late tox. from previous radiotherapy</li>
- > 12 months since previous radiotherapy
- ECOG ≤ 2



#### Hvordan har det gått?

- 3/5 har residivert. En "in-field" og to både "in-field" og regionalt.
- Til sammenlikning: 9 fått konvensjonell strålebehandling. 3 residiv. 3 døde innen et år av tox/komorbiditet(?). 3 residivfrie. Korteste oppfølgingstid 16 mnd.

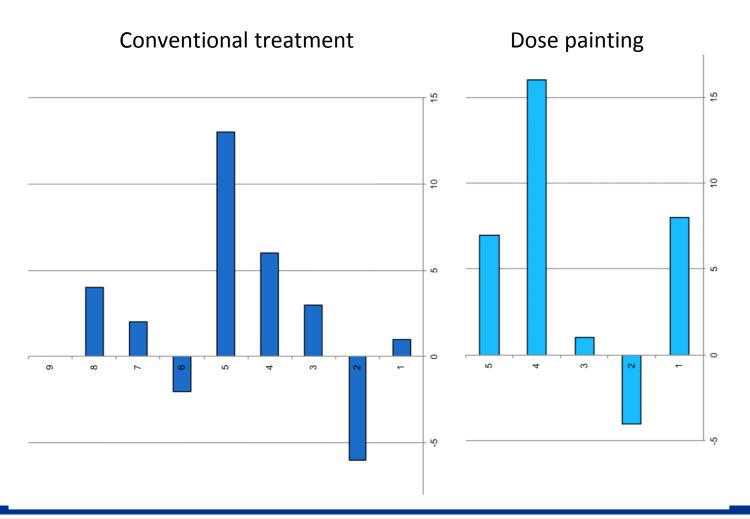


#### Hvordan har det gått?

- 5 behandlet siden juni -16. Siste mars -17.
- Ca 10 rebestrålingspasienter (uopererte) pr år. (10 opererte henvist for rebestråling.)
- Dose painting teknikken krever at minste diameter på tumor er ca 2 cm.



# Difference in score between baseline and two months after treatment, summed values for all parameters







#### Stereotaksi

- Ikke en leveringsteknikk, men et 'behandlingskonsept'
- Små veldefinerte målvolum
- Høy fraksjonsdose
- En eller få fraksjoner
- Høy presisjon
- Spesialtilpassede behandlingsapparater
- ... tillater/ønsker inhomogen dose i målvolum (130-150%)





#### Hva kan/bør behandles stereotaktisk?

- Små, ofte inoperable tumorer
- Historisk: Kun for intrakranielle indikasjoner (gliom, meningion, AVM, hjernemetastaser)
- Siste ca 20 årene: Også for ekstrakranielle indikasjoner
  - Lunge
  - Lever
  - Skjelett
  - Hode/hals
  - Prostata
  - Nyre





#### Stereotaktisk strålebehandling - hode- halskreft

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Phase II trial

## Multi institutional phase II study of concomitant stereotactic reirradiation and cetuximab for recurrent head and neck cancer



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#### Research group – dose painting

- Einar Dale, project leader
- Cecilie Amdal, oncologist
- Morten E Evensen, dosimetrist
- Torbjørn Furre, med. phys.
- Eirik Malinen, med. phys.
- Ayca Løndalen, nucl. med.
- Lars Tore G. Mikalsen, nucl.med.phys.



