Back to the future: history of imaging in Radiation Oncology

Vincent GREGOIRE, MD, PhD, hon. FRCR (UK, IE)

Radiation Oncology Department, Centre Léon Bérard, Lyon, France
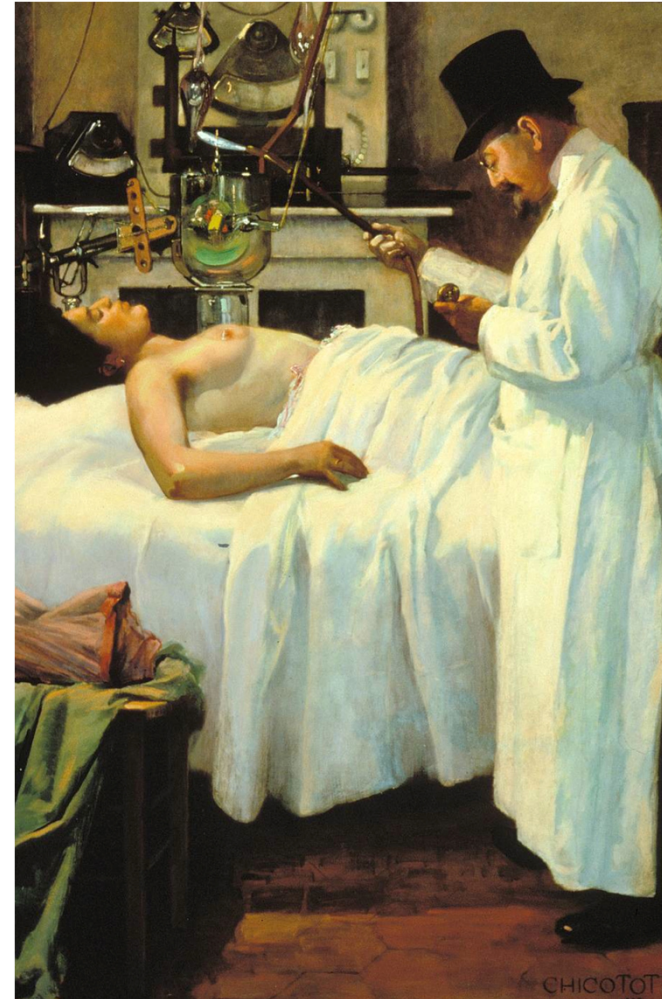
Roma, Oct. 2023

A journey from medical art …

… to personalized Radiation Oncology

The invaluable role of imaging

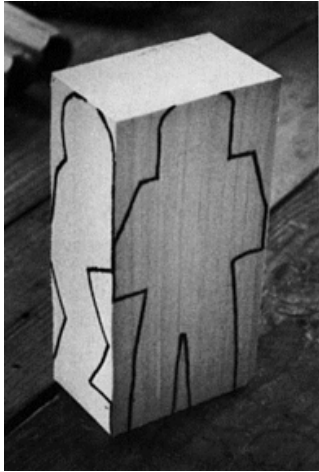CENTRE DE LUTTE CONTRE LE CANCER
LEON BERARD

Roma, Oct. 2023

From medical art …

Discovered in 1895 and immediately used for the treatment of cancer… Why so quickly? Surgery was the only option but it was not armless…

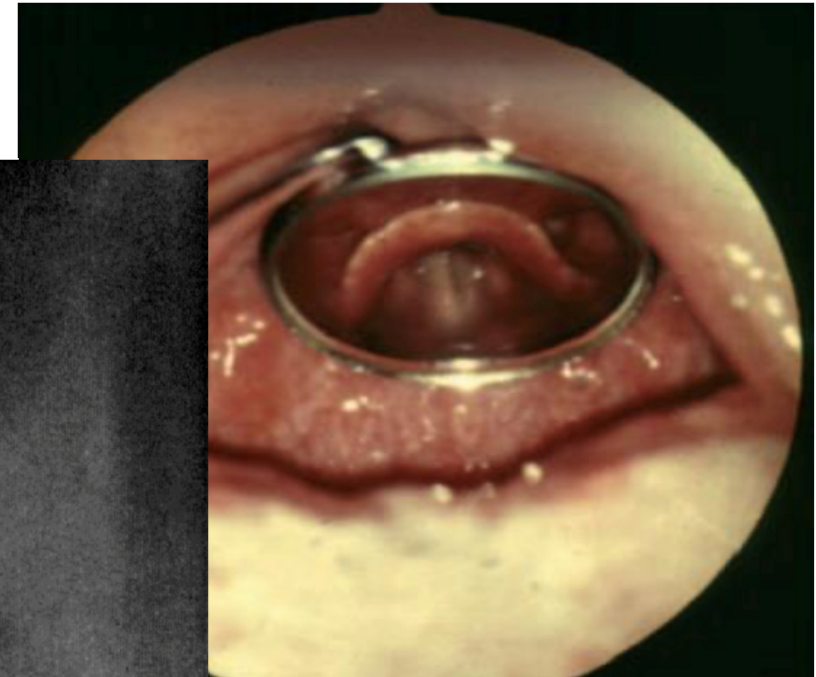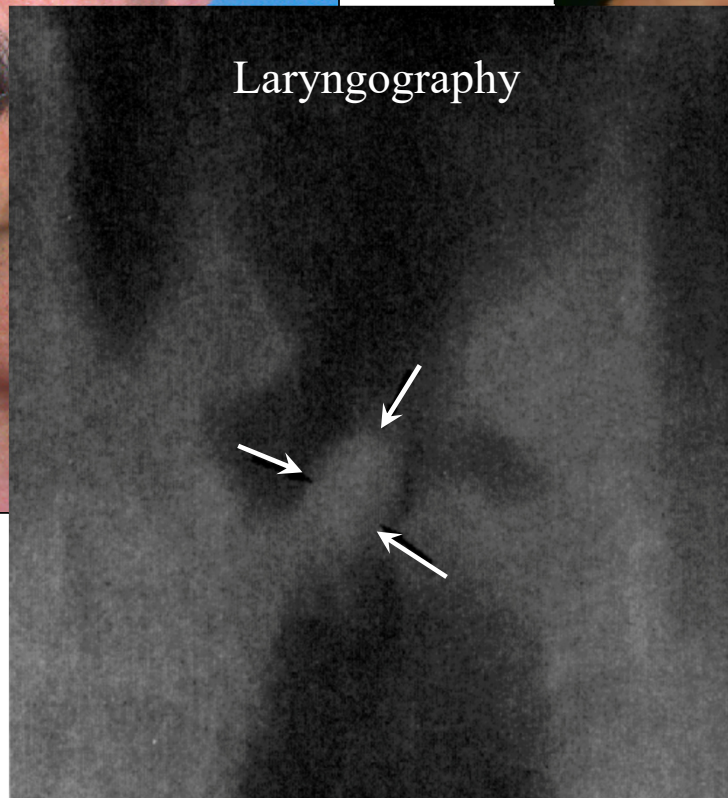CENTRE DE LUTTE CONTRE LE CANCER
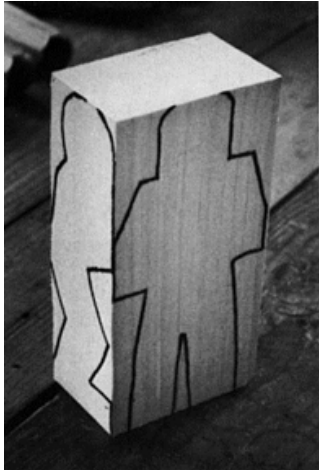LEON BERARD

First steps of radiotherapy…
Clinical imaging

"1-D imaging"

< 1950

Laryngography

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

"1-D treatment"

< 1950

First steps of radiotherapy…
"Medical art"

Curie Institute, Paris / T1-T3 (?) laryngeal tumor / 180 kV X-Ray / 3800-8600 R

LOCATION	1919–1939		1940–1946		TOTAL 1919–1946	
	Treated	Clinically Healed	Treated	Clinically Healed	Treated	Clinically Healed
Vestibulum and ventricular cavity	80	11	70	16	150	27
Limited cord	15	7	11	10	26	17
Extensive cord	96	15	49	22	145	37
Subglottis	10	1	2	1	12	2
Total	201	34	132	49	333	83
Percentage	17		37		25	

Baclesse, J. Faculty Radiologist, 1952

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
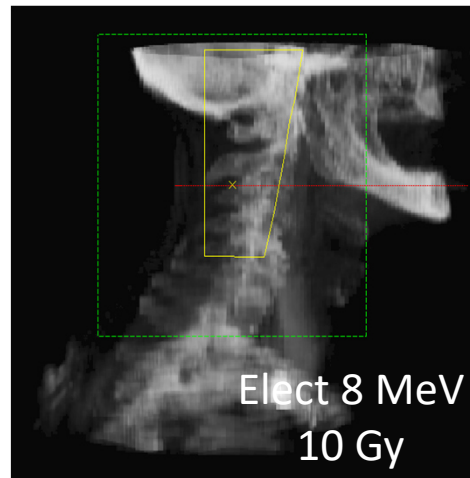
"1-D Imaging"
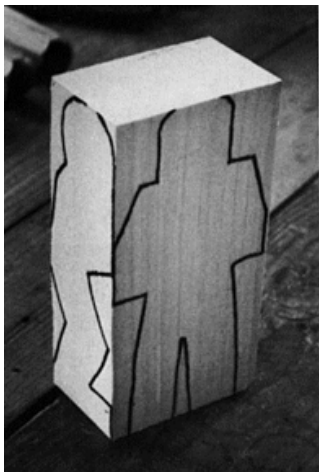
< 1950

2-D Imaging
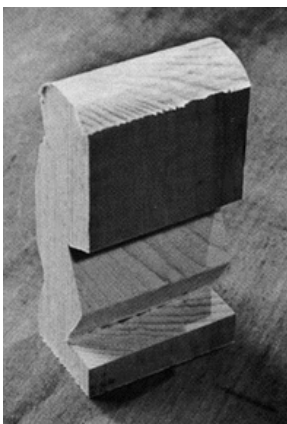
≈ 1960

Some progresses…

PROTOTYPE du 1er SIMULATEUR
LEUVEN, 1967.
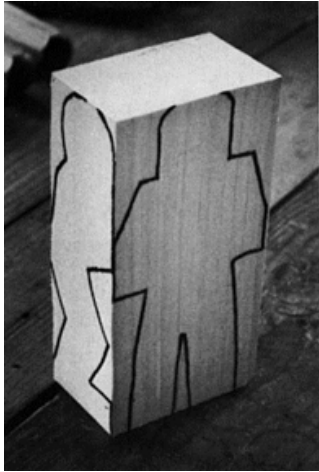
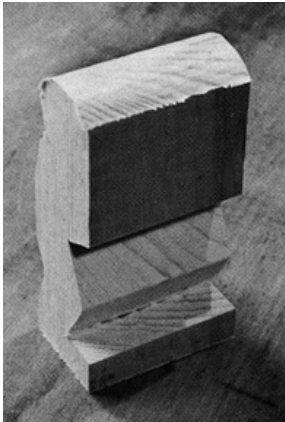Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

"1-D treatment"

< 1950

2-D treatment

≈ 1960

Some progresses…

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
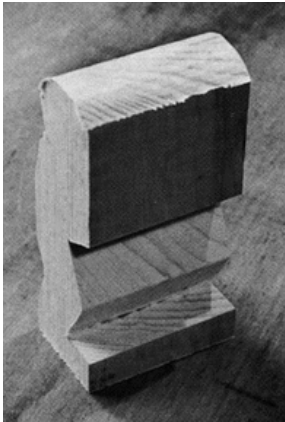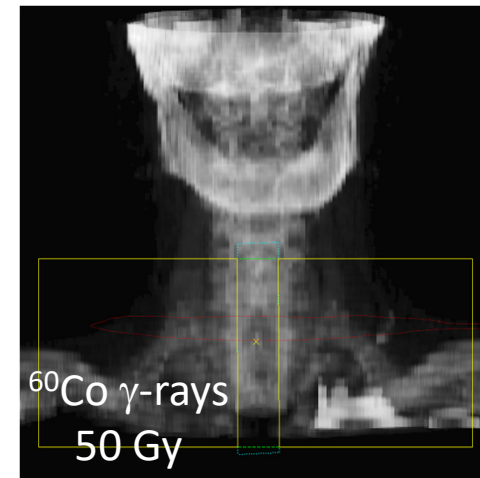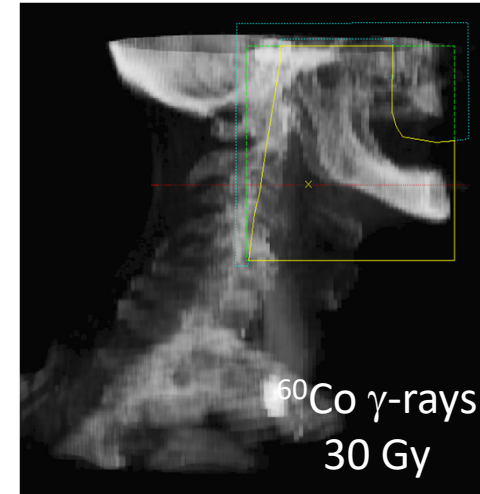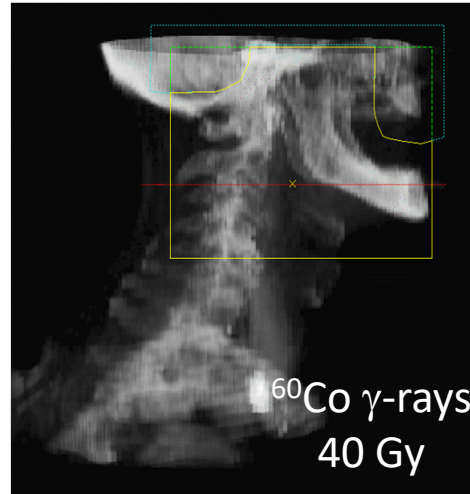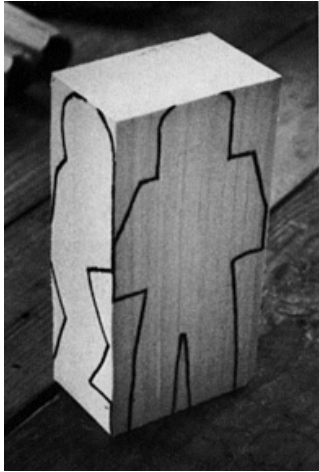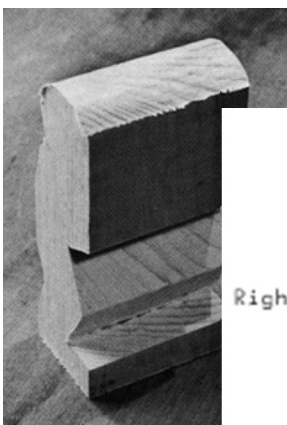
"1-D treatment"

< 1950

2-D treatment

≈ 1960

Some progresses…
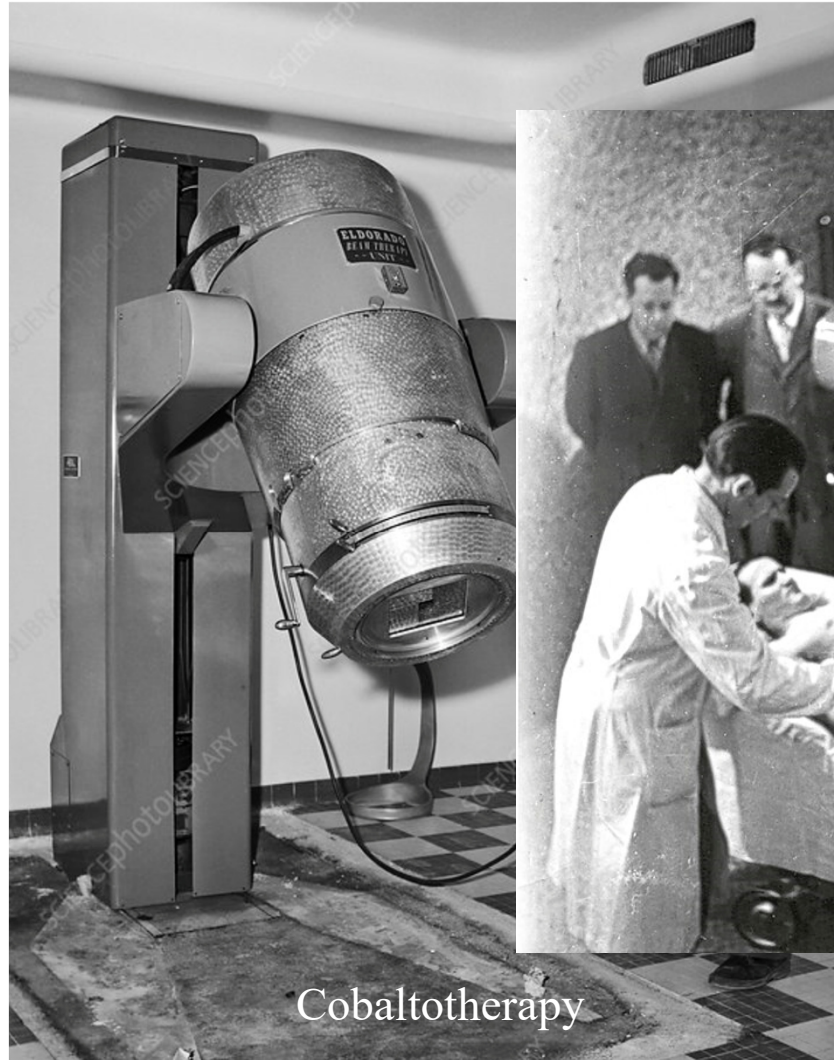
Cobaltotherapy

Cobalt therapy in Borgo Valsugana, Italy, 1953

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
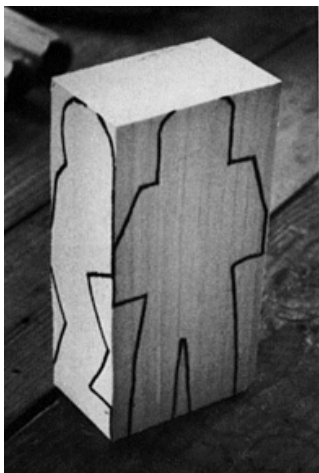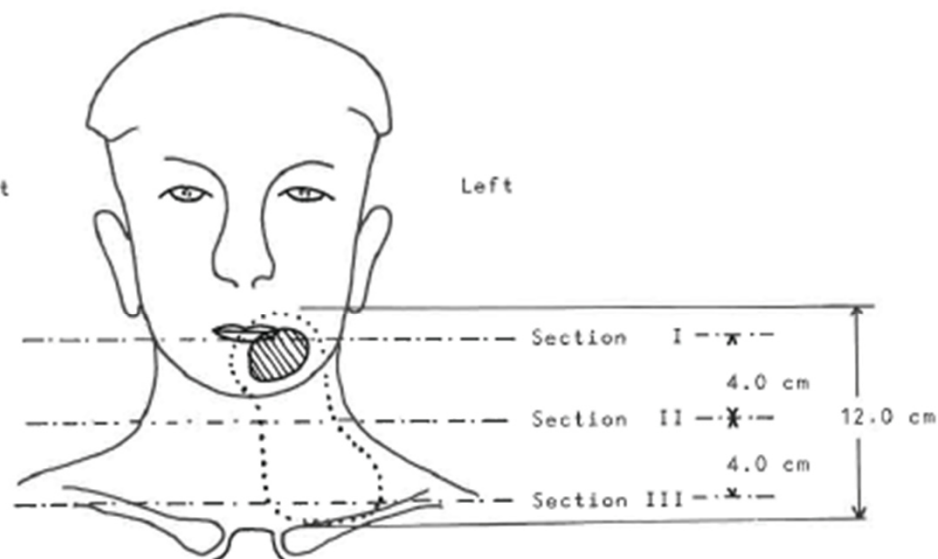
"1-D treatment"

< 1950

2-D treatment

≈ 1960

Some progresses…

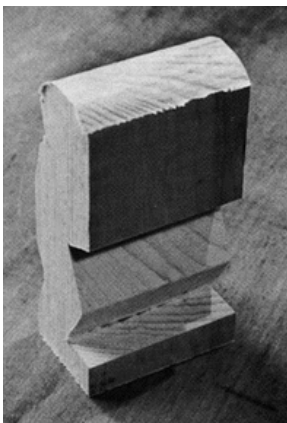Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

"1-D Imaging"

< 1950

2-D Imaging

≈ 1960

3-D Imaging

≈ 1990

Some progresses…

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
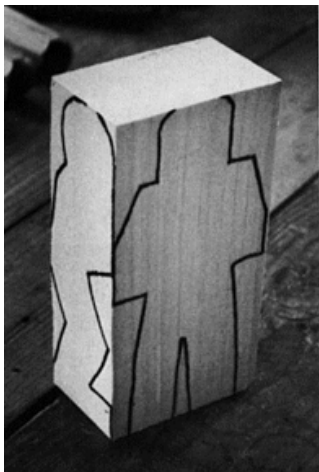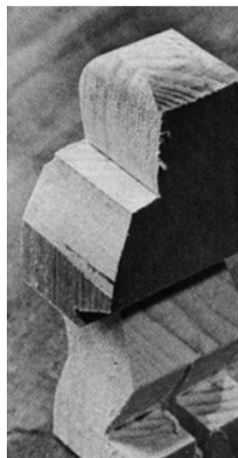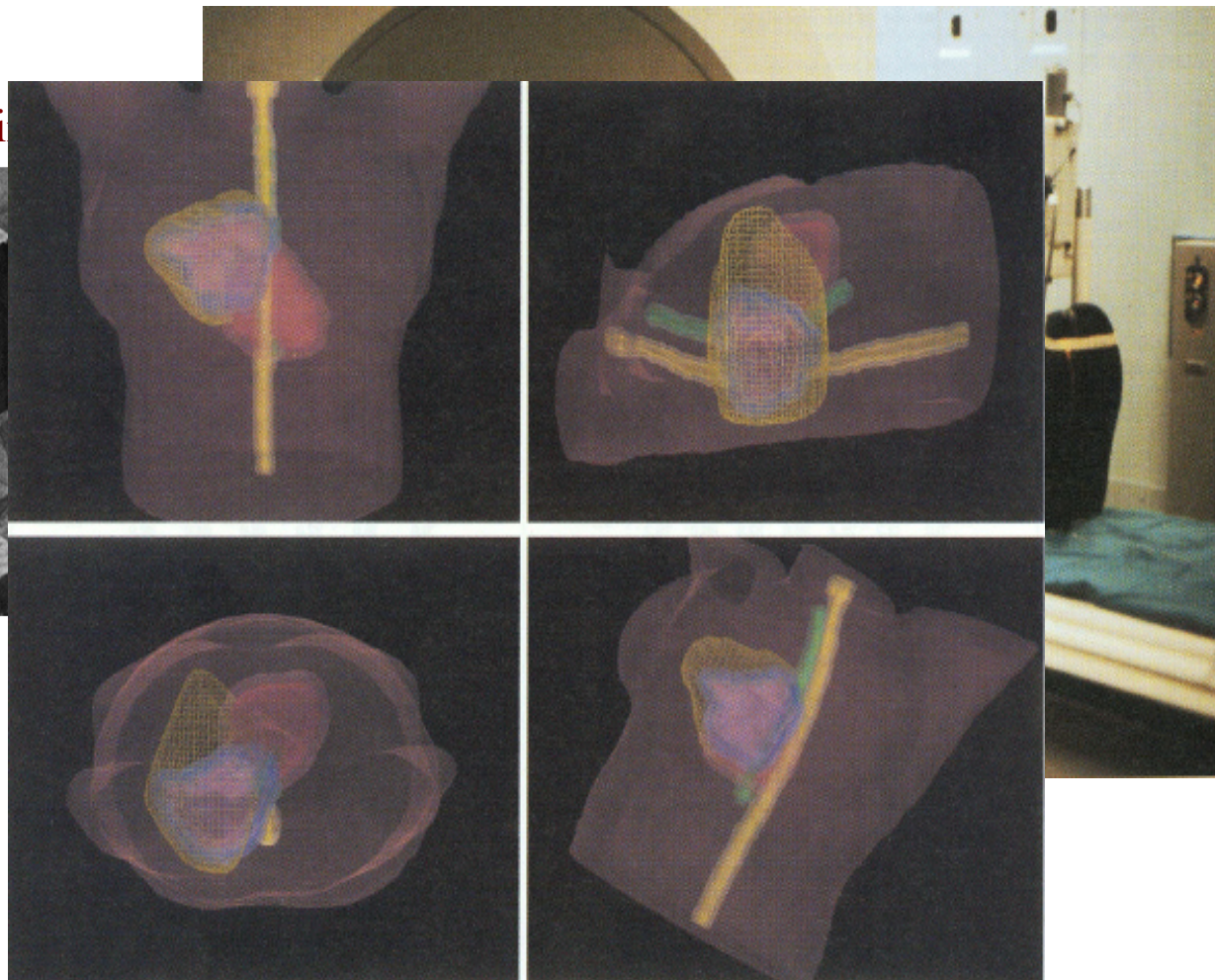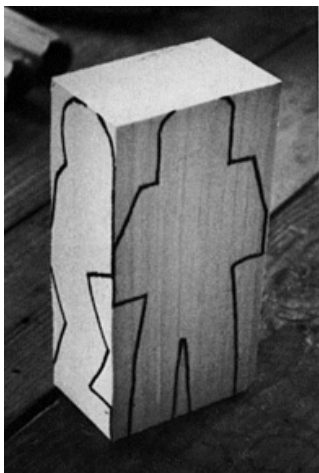
"1-D treatment"

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2-D treatment

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3-D treatment

≈ 1990

Some progresses…

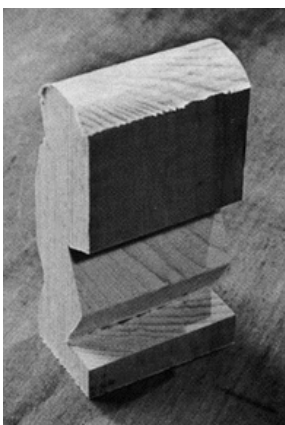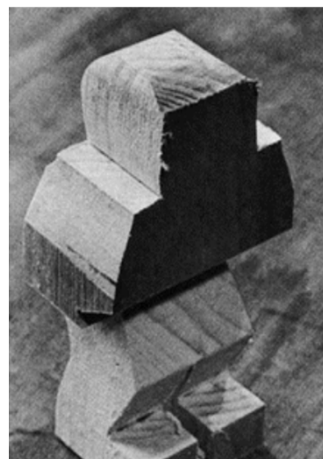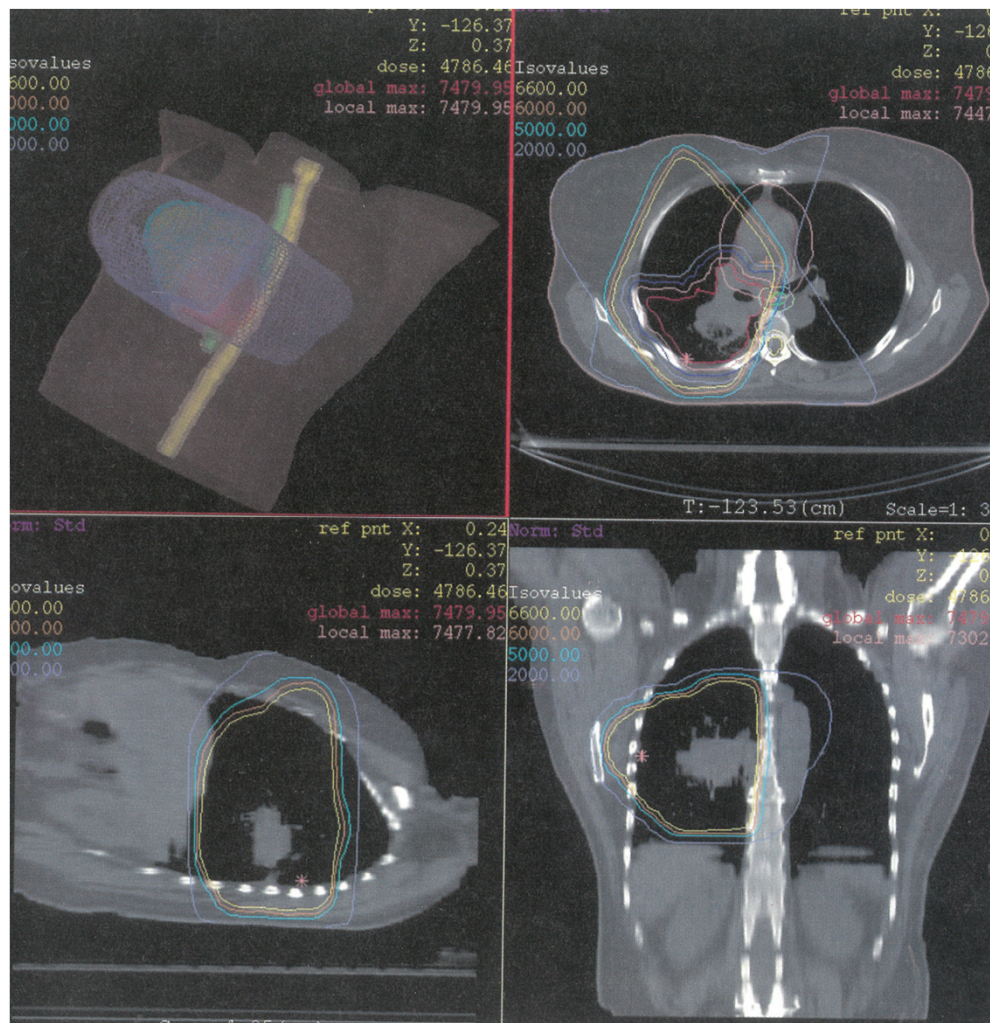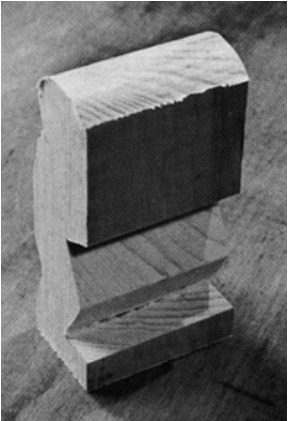Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

Some progresses…

"1-D Imaging"

< 1950

2-D Imaging

≈ 1960

3-D Imaging

≈ 1990

Multimodality Imaging

≈ 2000

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
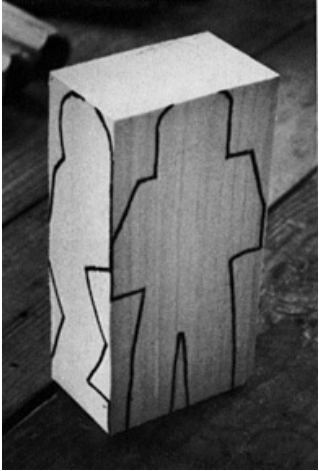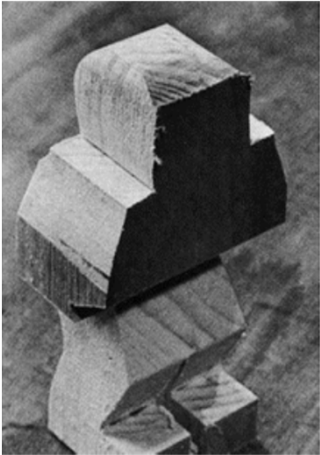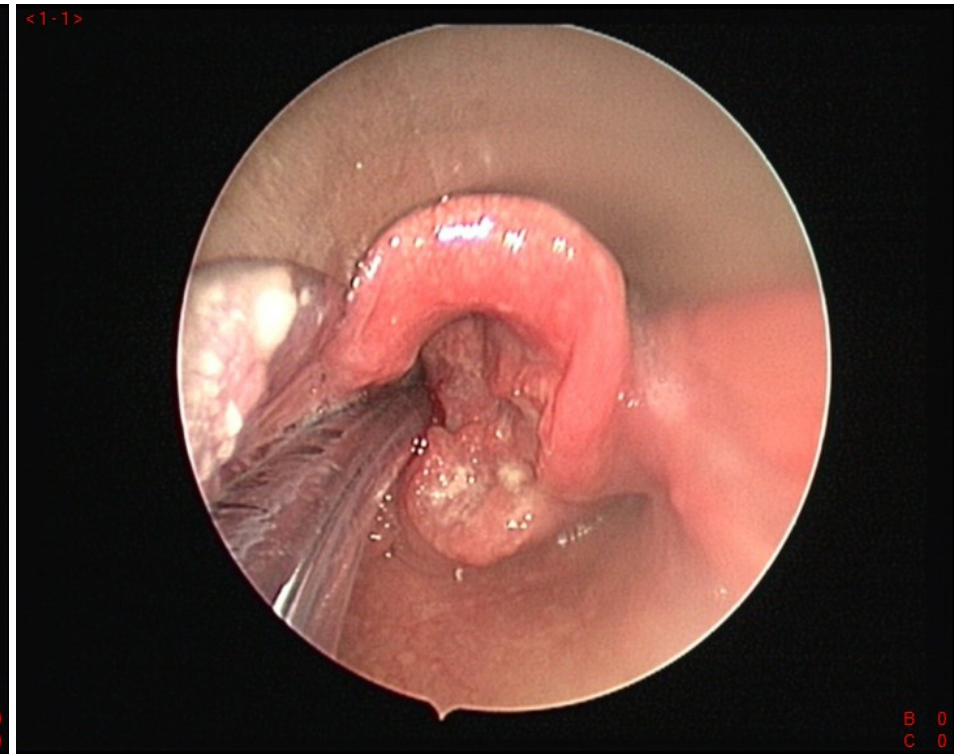
Target volume: clinical examination
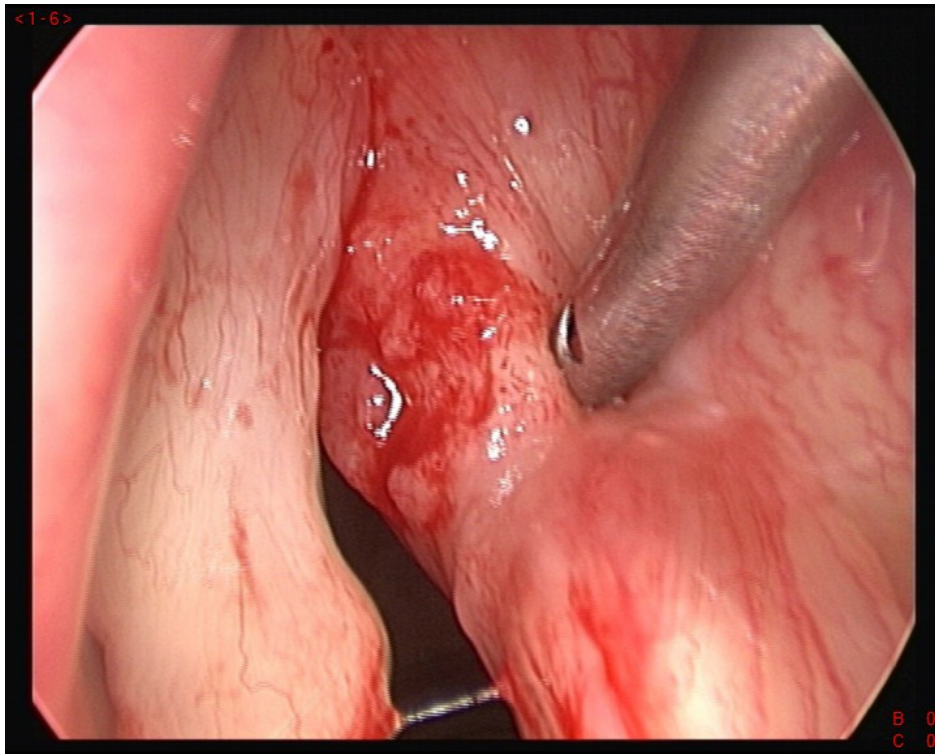
T1a glottic larynx

T3 supra-glottic larynx

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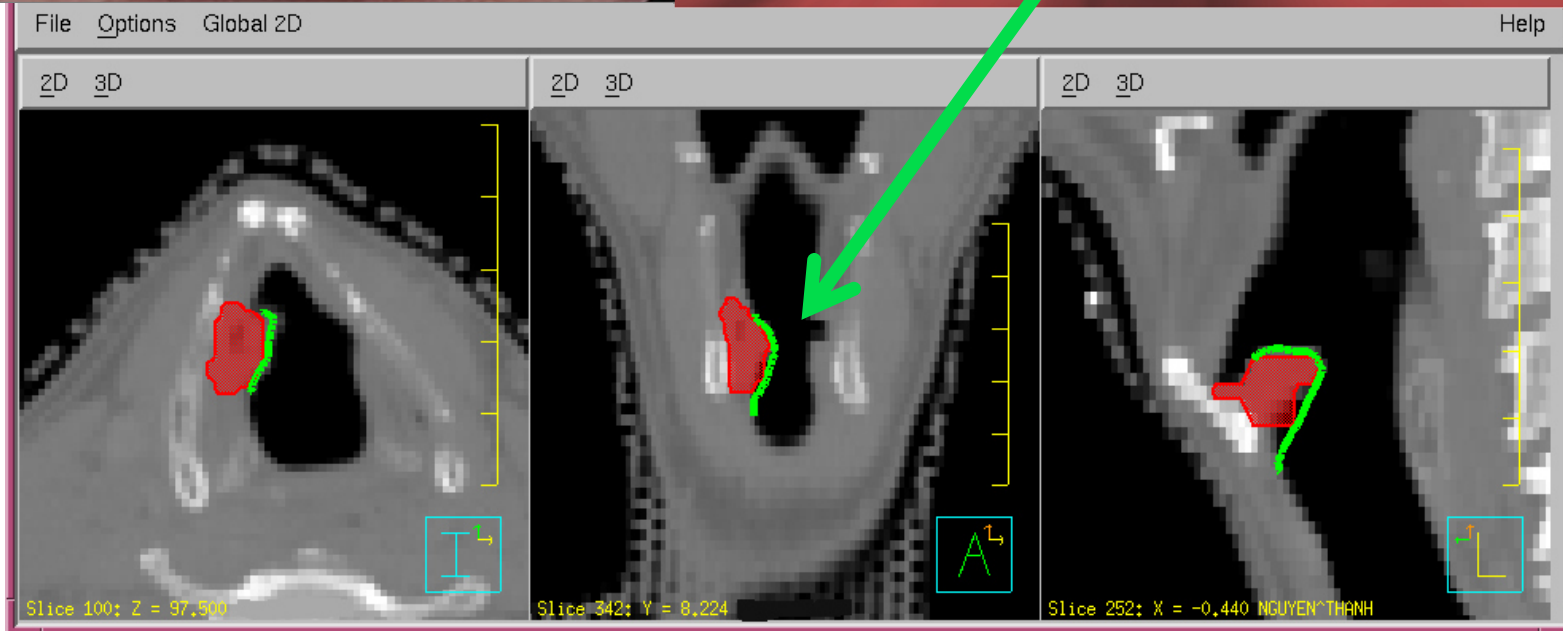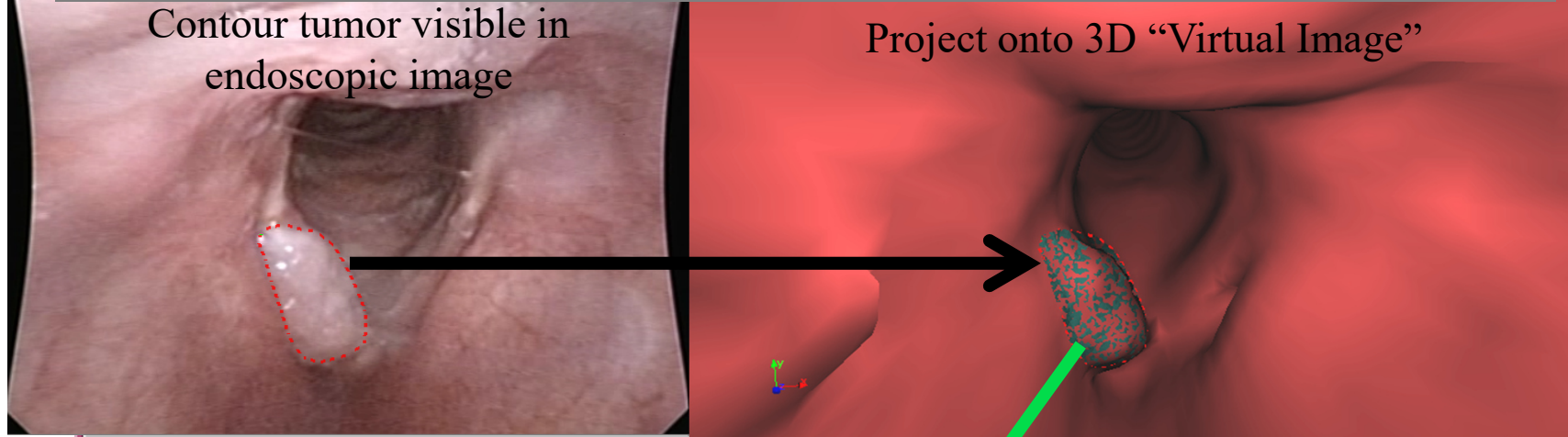
Clinical Impact: Endoscopic Contouring

Contour tumor visible in endoscopic image

Project onto 3D "Virtual Image"

Weersink et al Med. Phys 38 6458, 2011   Weersink, US Patent: 9,138,597

Multimodality imaging for target visualisation
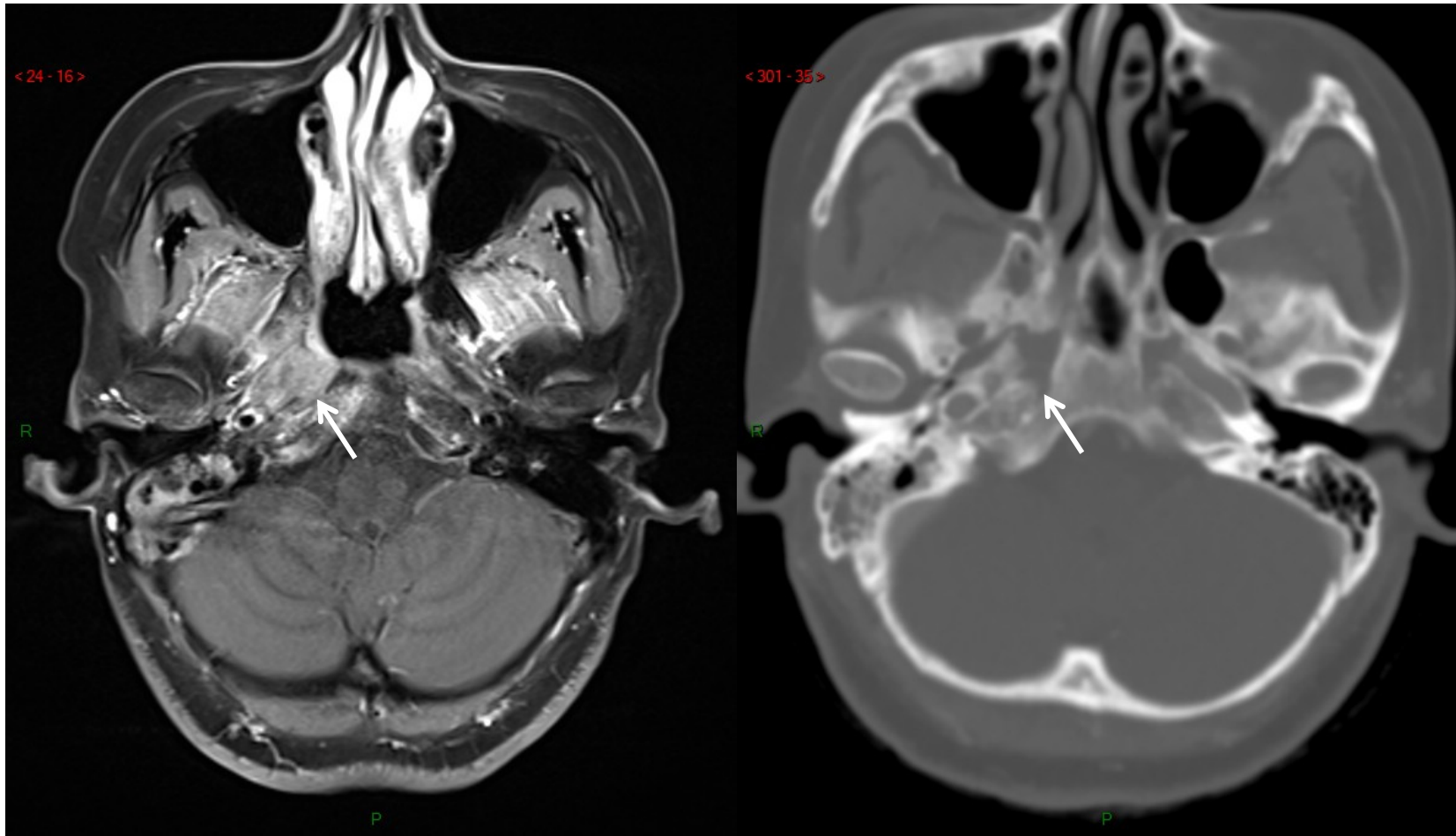
Gadolinium-enhanced T1 FatSat   Contrast-enhanced CT (bone window)

Courtesy of Th. Duprez

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Multimodality imaging for target visualisation

Anatomic
&
molecular
imaging

Roma, Oct. 2023

Courtesy of X. Geets

Multimodality imaging for target visualisation

Anatomic & molecular imaging

CE-CT

^{11}c-methionine

T1-MRI
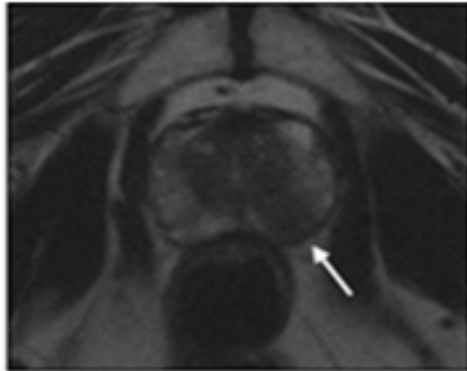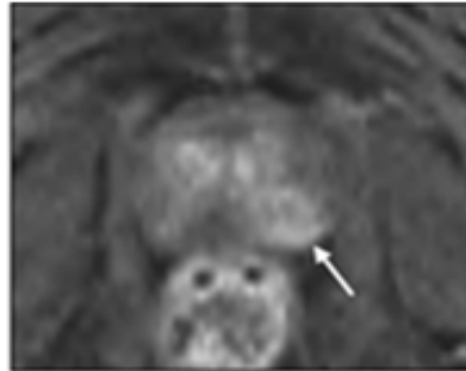
FLAIR-MRI
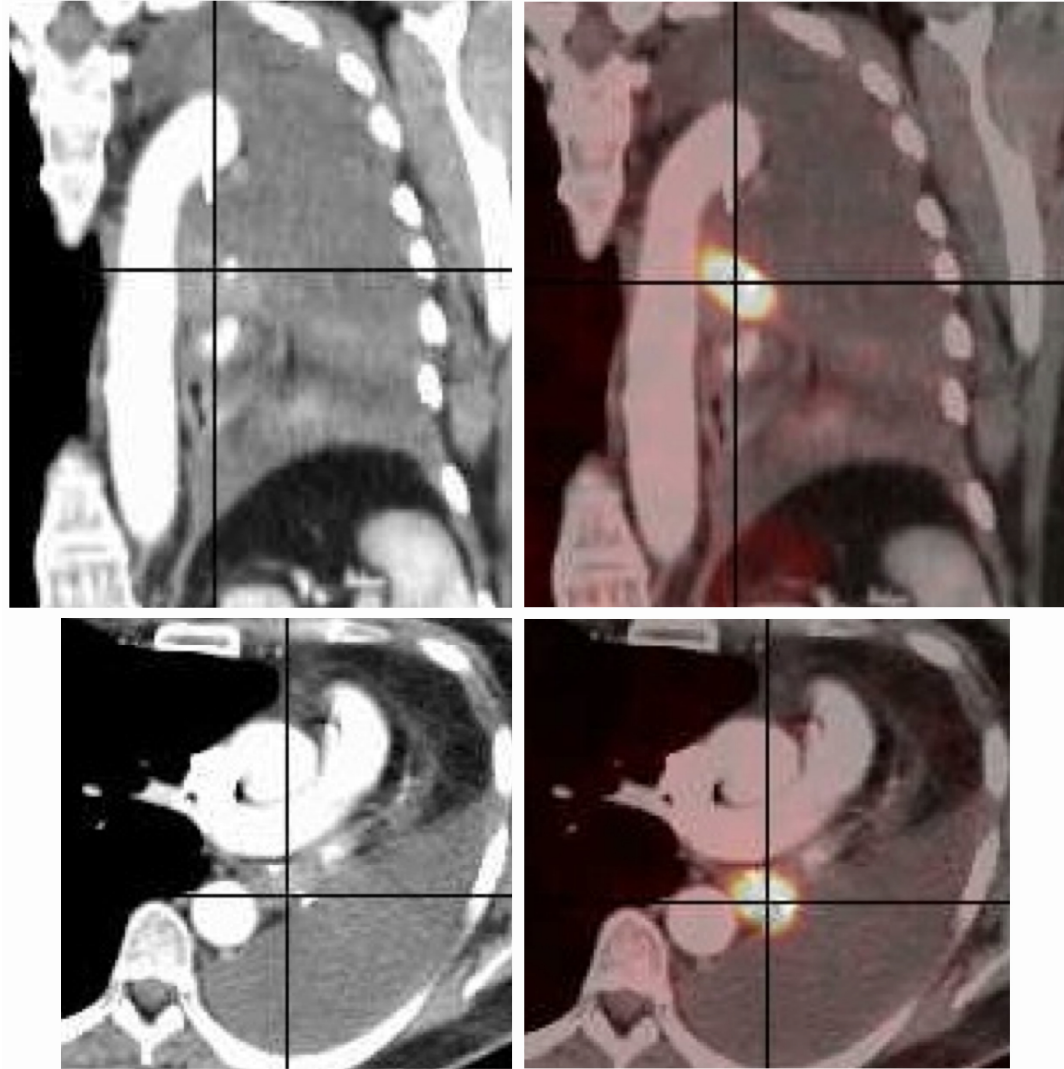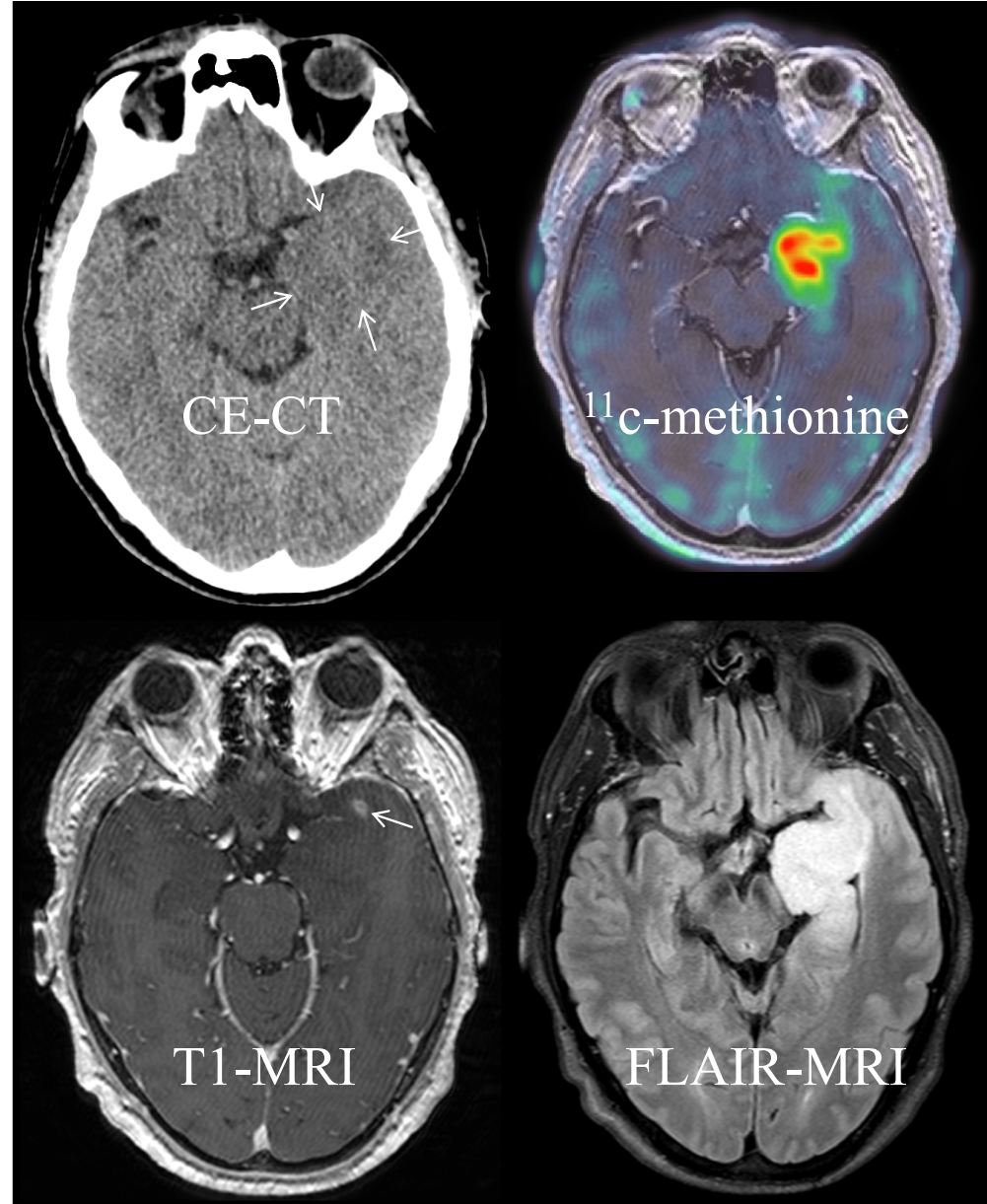
Courtesy of L. Renard

Multimodality imaging for target visualisation
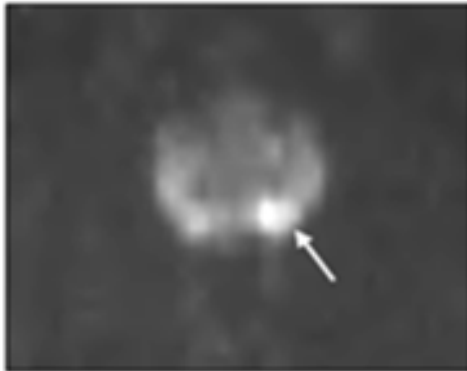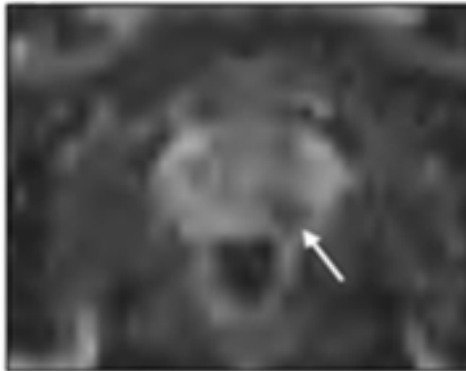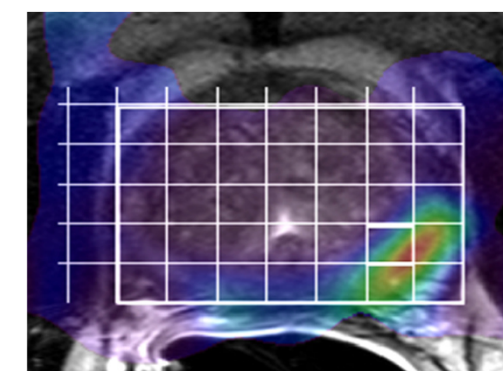

T2w MRI

DCE MRI

[11]C-Choline PET-CT
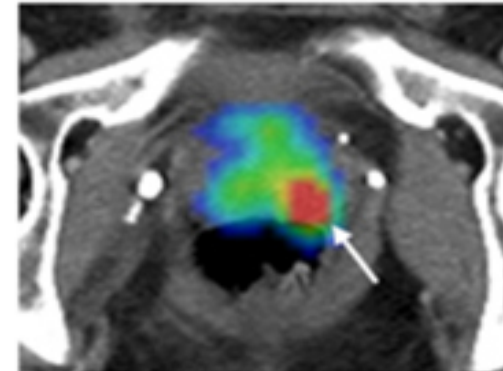
DW MRI: b1000
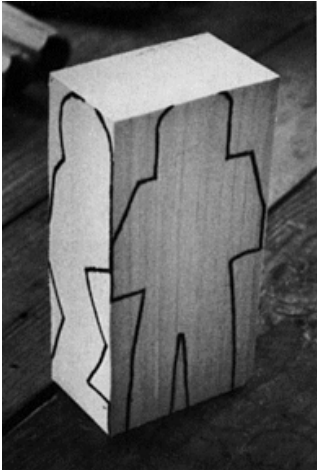
DW MRI: ADC map

MRS

Roma, Oct. 2023

Courtesy of K. Haustermans

"1-D treatment"

< 1950

2-D treatment

≈ 1960

3-D treatment

≈ 1990

IMRT/VMAT

≈ 2000

Some progresses…

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
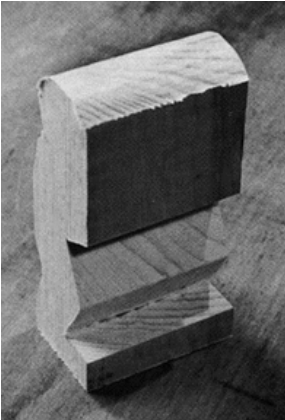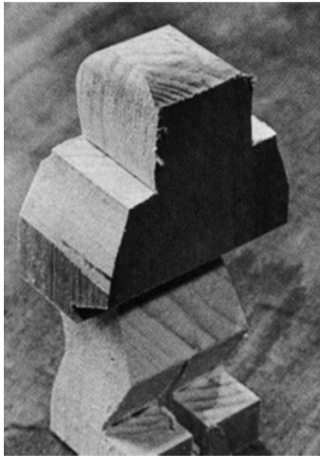
Thirty years of progresses: the Danish example
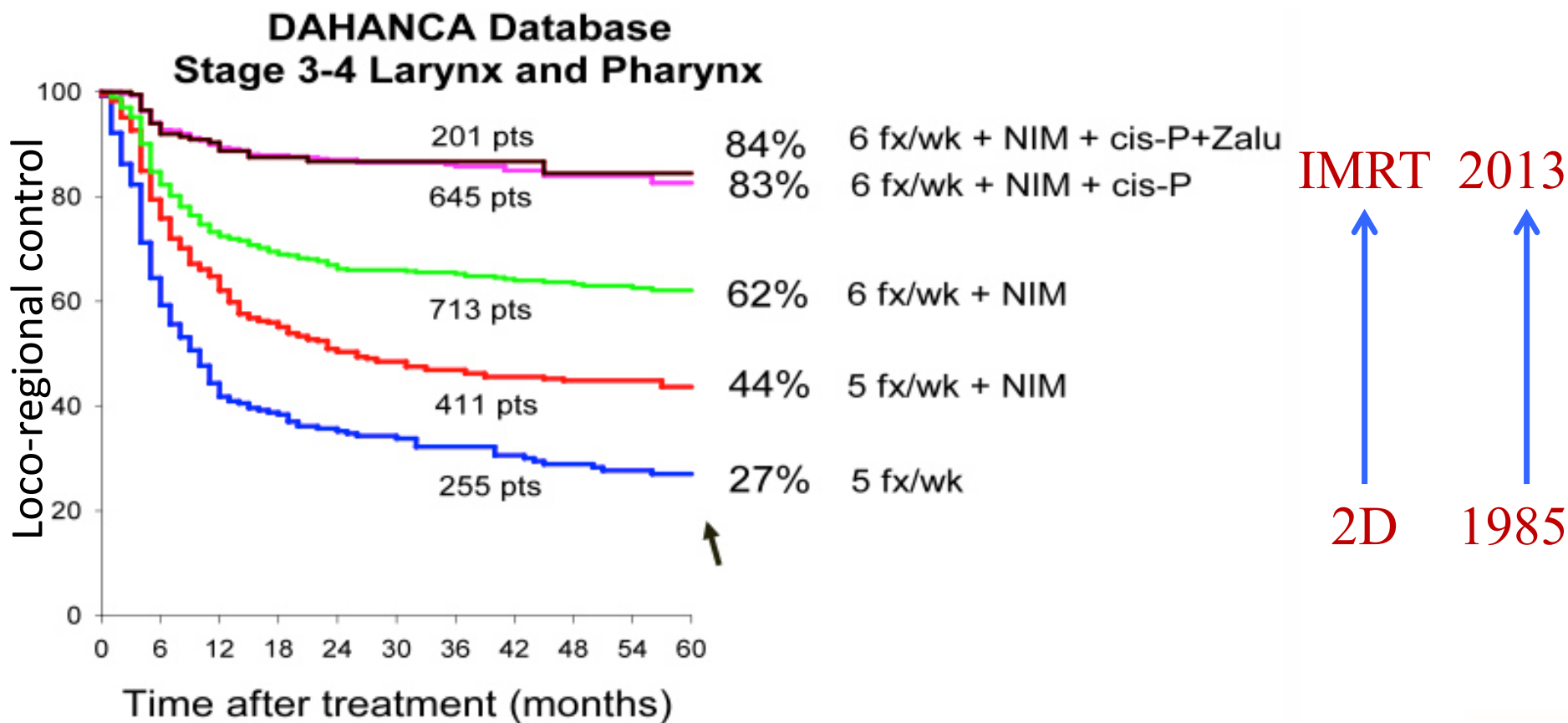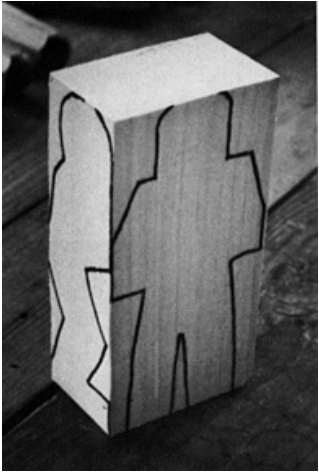
DAHANCA Database
Stage 3-4 Larynx and Pharynx

pts	%	treatment
201 pts	84%	6 fx/wk + NIM + cis-P+Zalu
645 pts	83%	6 fx/wk + NIM + cis-P
713 pts	62%	6 fx/wk + NIM
411 pts	44%	5 fx/wk + NIM
255 pts	27%	5 fx/wk

Loco-regional control vs. Time after treatment (months)

IMRT 2013

2D 1985

Roma, Oct. 2023

DAHANCA.dk

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Courtesy of Overgaard 2015

Some progresses…

"1-D Imaging"

< 1950

2-D Imaging

≈ 1960

3-D Imaging

≈ 1990

Multimodality
Imaging

≈ 2000

Molecular
Imaging

≈ 2010

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
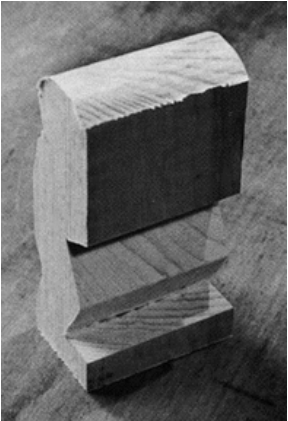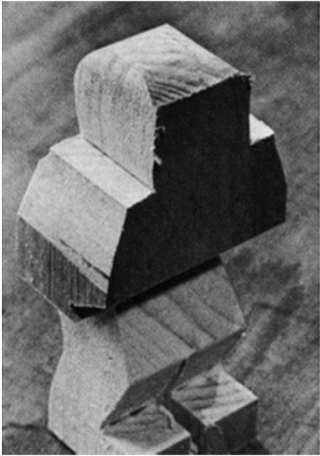
DW-MRI as surrogate of cell density?

RxTh

Good response: high ΔADC

Radioresistence: low ΔADC

CENTRE DE LUTTE NTRE LE CANCER LEON BERARD

Courtesy of S. Nuyts
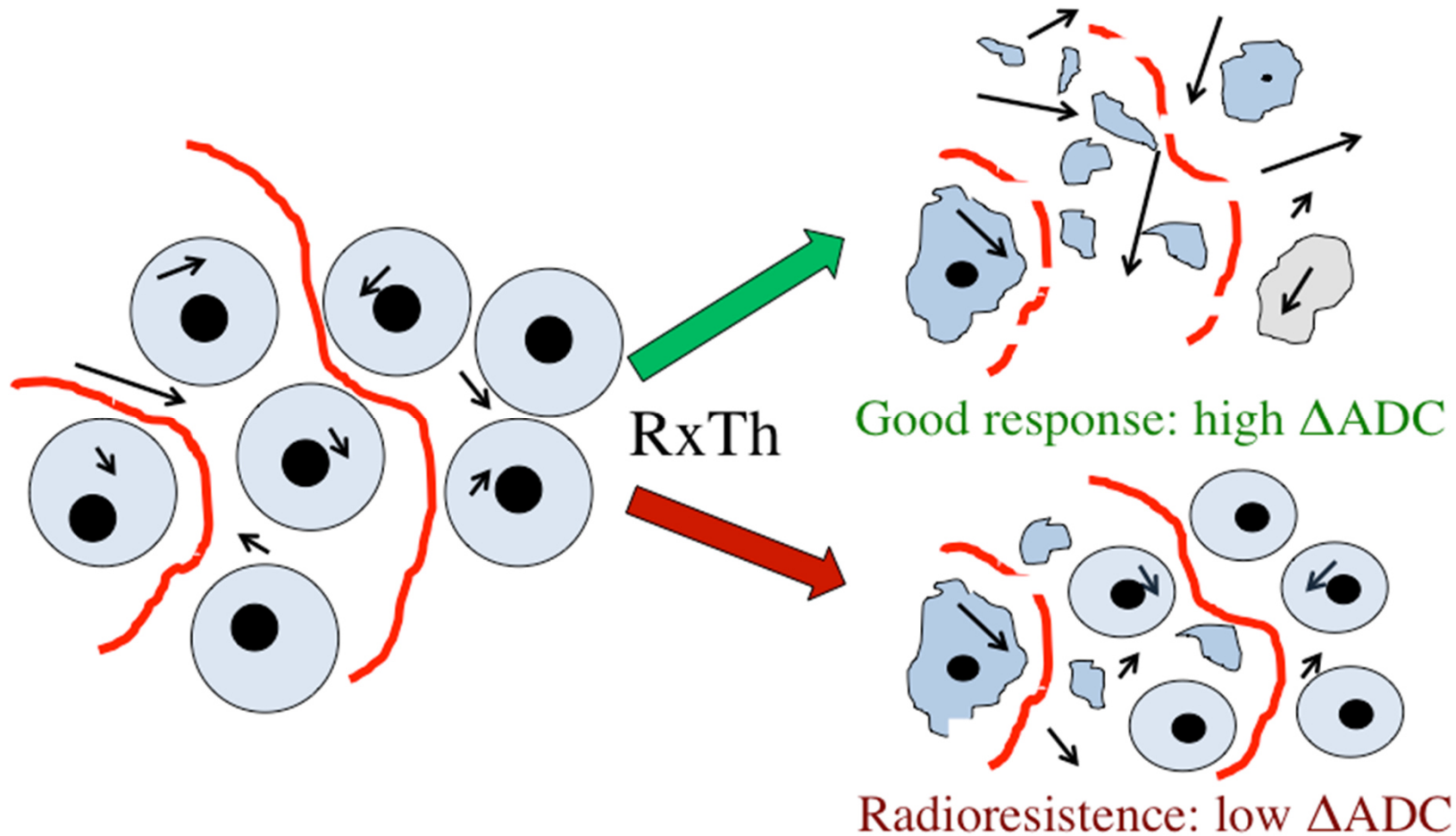
DW-MRI as surrogate of cell density?

Correlation between cell density and ADC value in 17 patients with WHO I-IV glioma

Ellingson et al, JNMR, 2010
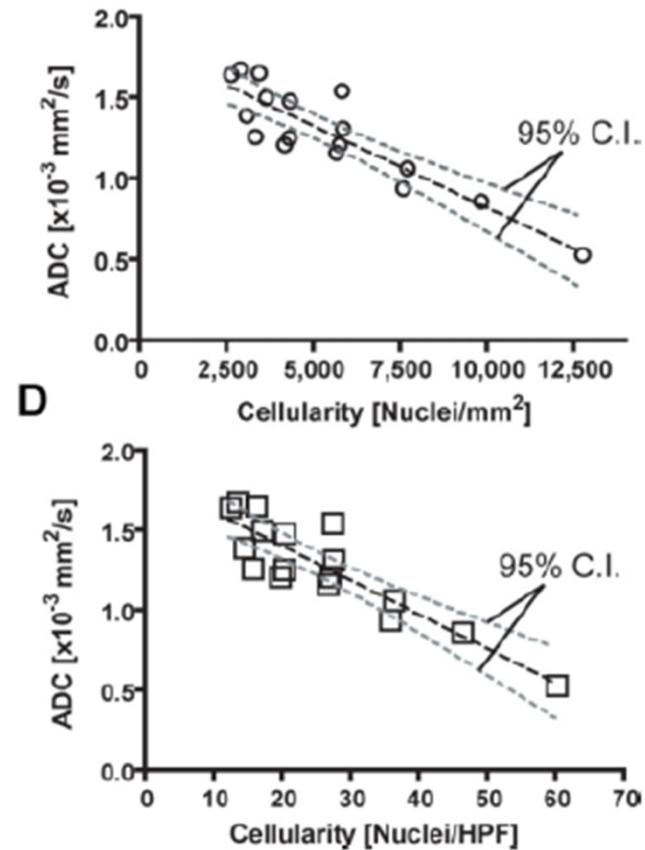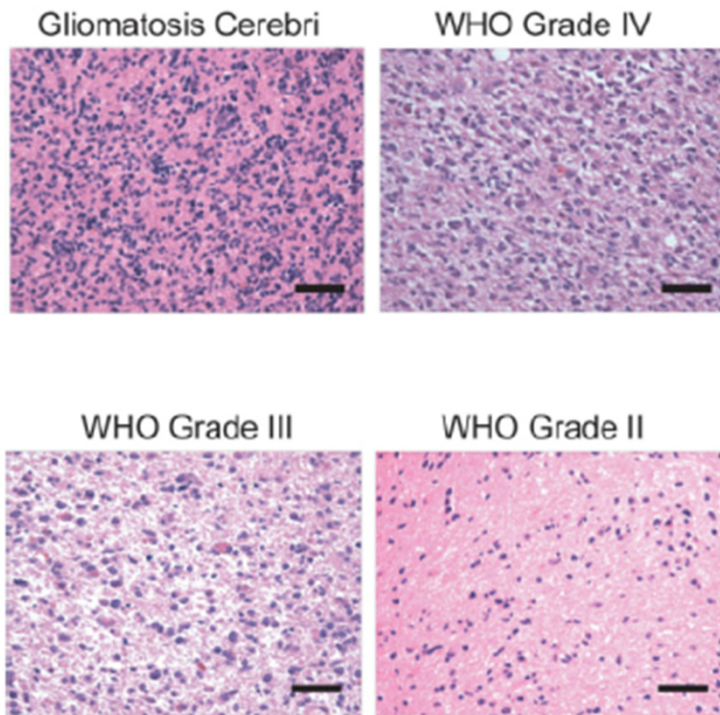
Validation of molecular imaging: comparison between ^{18}F-FAZA PET and EPR oximetry
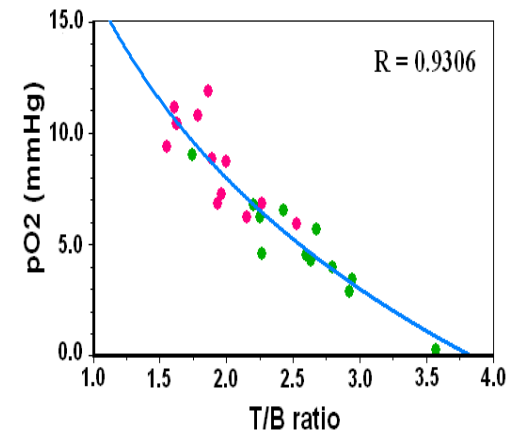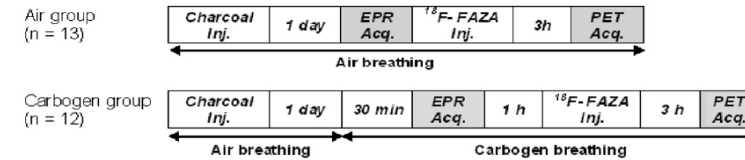
Accumulation increases under 10 mm Hg
(radiobiologically relevant hypoxia)

Comparison between ^{18}F-FDG PET and ^{14}C-EF3 auto-radiography

N. Christian, R&O, 2010
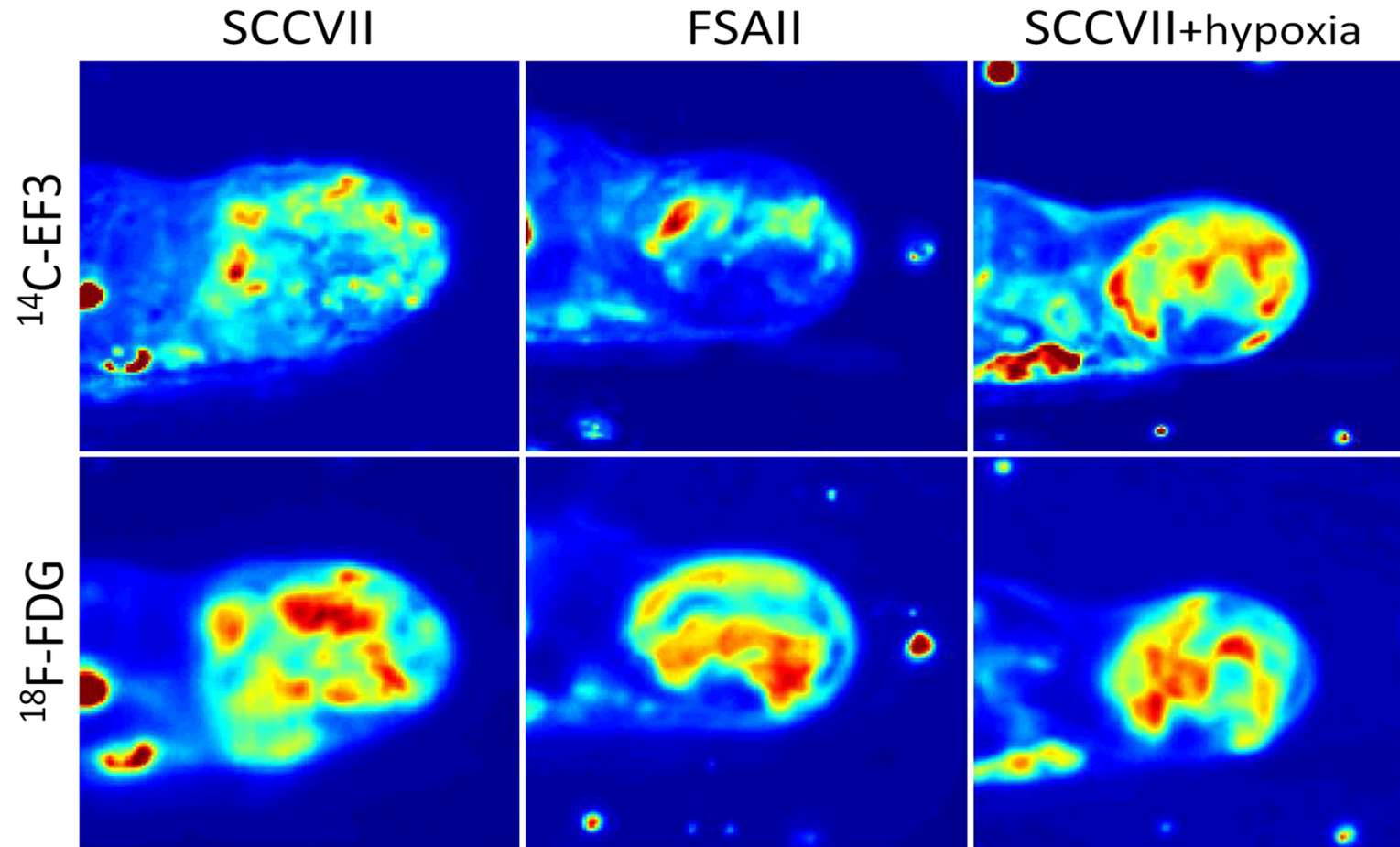
Tumor heterogeneity on imaging
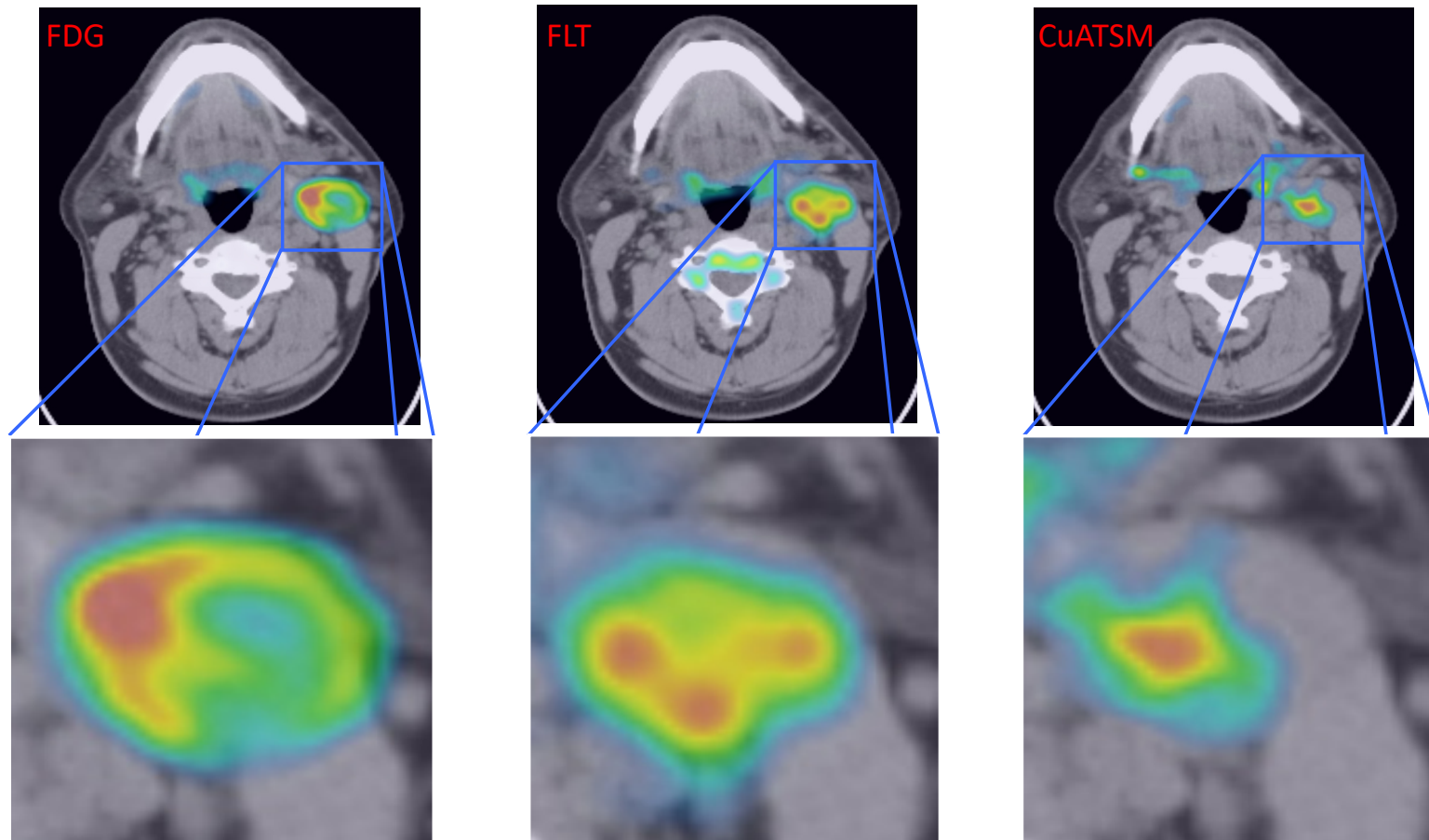
FDG   FLT   CuATSM

Roma, Oct. 2023

Jeraj *et al*, 2010

Some progresses…

"1-D treatment"

< 1950

2-D treatment

≈ 1960

3-D treatment

≈ 1990

IMRT/VMAT

≈ 2000

Dose Painting

≈ 2010

Roma, Oct. 2023

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario
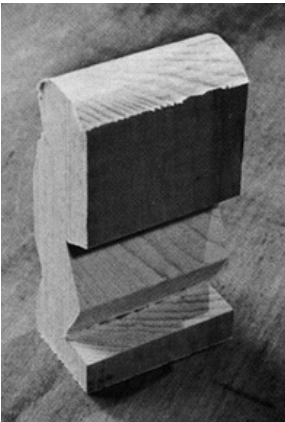
Spatial accuracy of modern imaging equipment (data on phantom)

Imaging modality	Spatial accuracy
CT scanner	≈ 0.3 mm
MRI scanner	≈ 1 mm
PET-CT	≈ 4-5 mm

Siemens, data on file; Slomka *et al*, Sem Nuc Med, 2016; Wong *et al*, Quant Imaging Med Surg 2017

CENTRE
DE LUTTE
CONTRE LE CANCER LEON
BERARD

An image …

Ceci n'est pas une pomme

<u>Betrayal of images</u>

This is not an apple…

R. Magritte, 1964

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

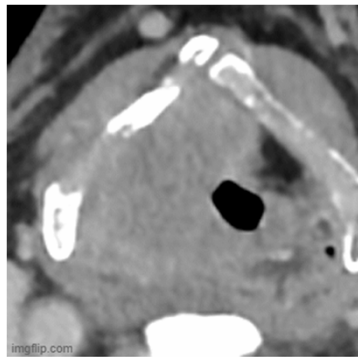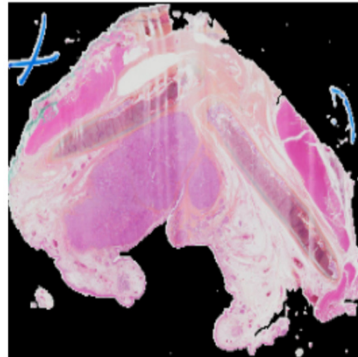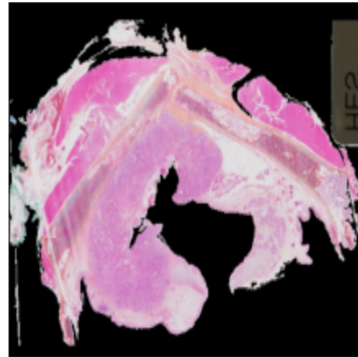# From primary tumor GTV to CTV
IA-based correlation between pathology and imaging
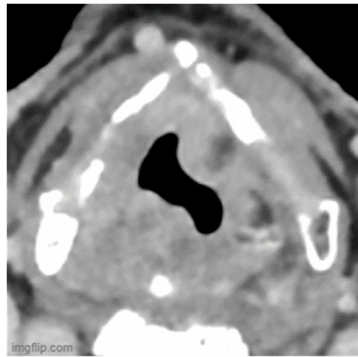
Registration of CT on pathology

Ground truth
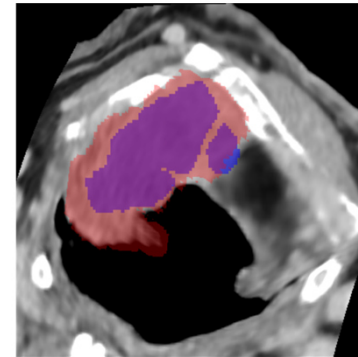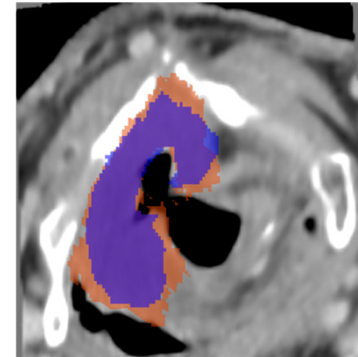
Registration of pathology on CT

Average GTV overestimation of ≈ 25%

Courtesy of A. Leroy, 2023

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Dose painting and geometric uncertainties

Effect of 5 mm translations and 3 mm blurring

E. Sterpin, 2013
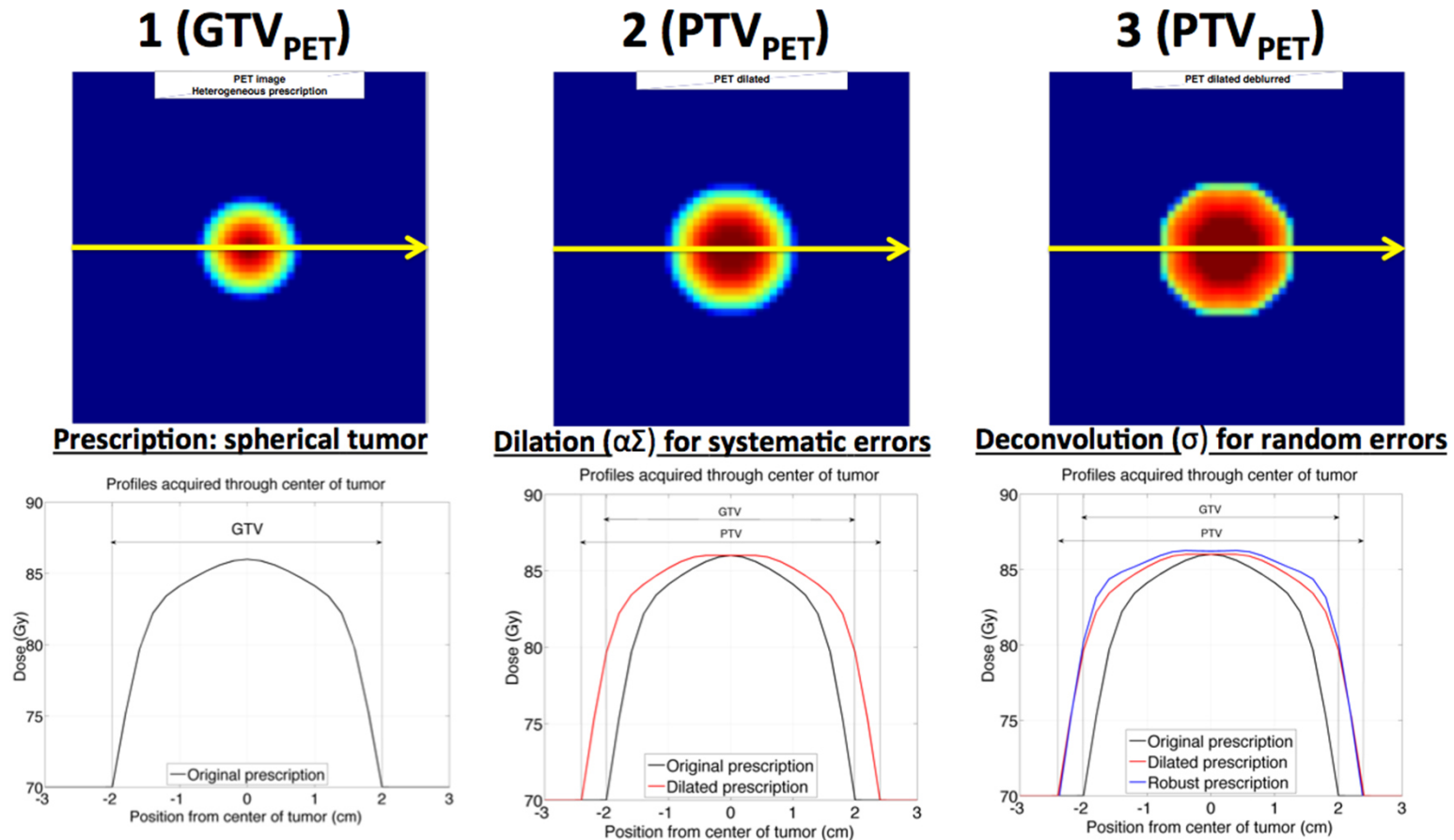
Dose painting and dose painting …

Dose Painting
By Number

→

Contour-driven
DPBN

(discretization of the dose-painted
volumes)

Randomized trials on dose painting / dose escalation in locally advanced HNSCC

Local control
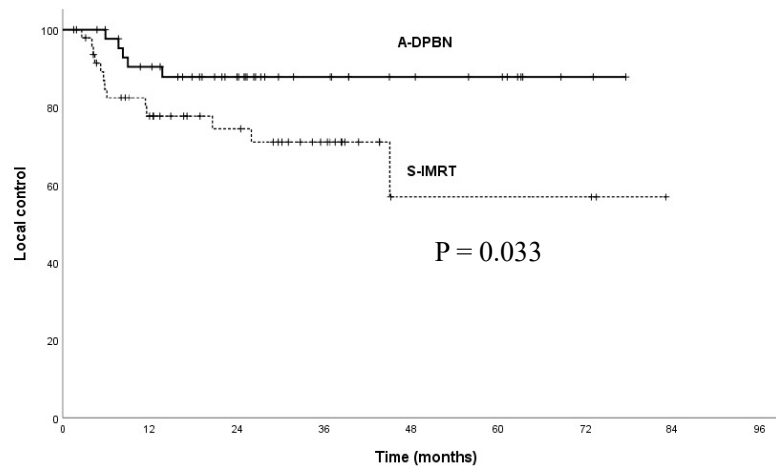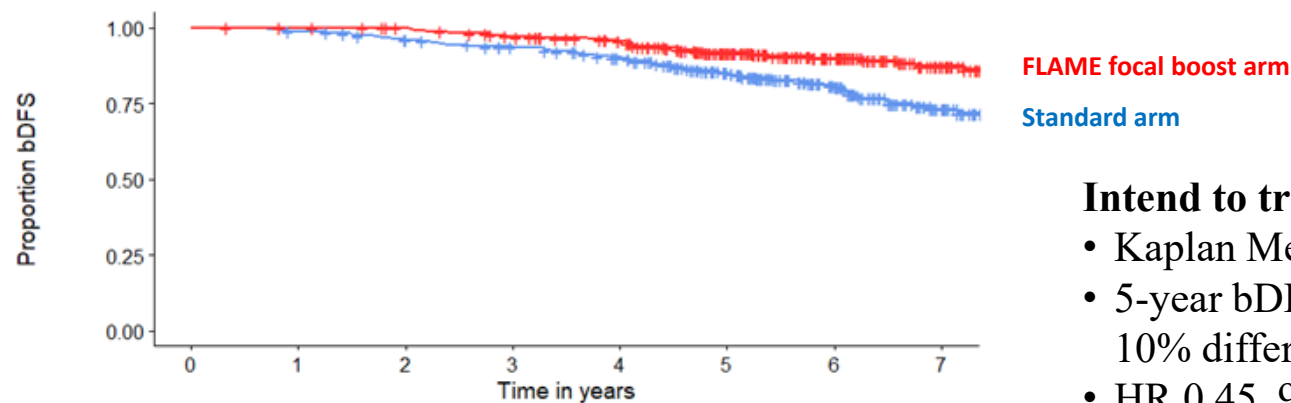
	A-DPBN	S-IMRT
1Y	91%	78%
2Y	88%	75%

P = 0.033

- FDG-PET planning
- Adaptive IMRT, FDG-PET W1&2
- Median dose of 69 Gy >< 81 Gy
- > 80 Gy in < 1.75 ml
- Late mucosal ulcer in active smokers and drinkers

Focal dose escalation for high-risk disease: the FLAME trial
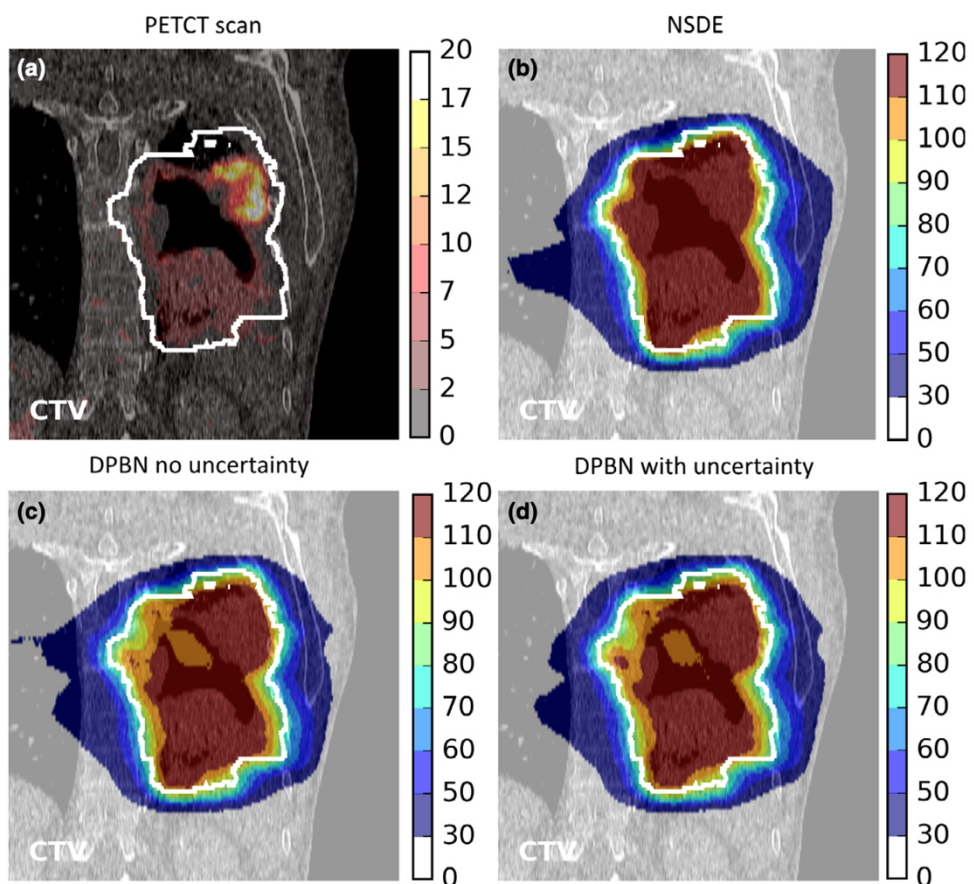
Biochemical disease-free survival

FLAME focal boost arm

Standard arm

Intend to treat:
- Kaplan Meier: log-rank p<0.001
- 5-year bDFS: 85% vs 92% (95%CI 4-10% difference)
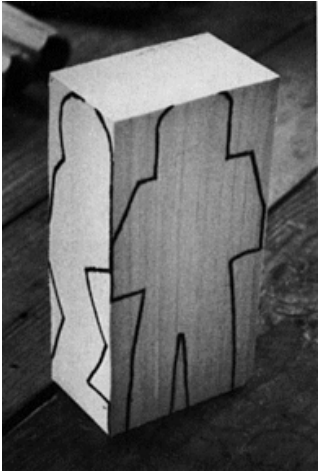- HR 0.45, 95% CI 0.28-0.71, p<0.001

Dose painting or non-selective dose escalation?

- 12 pts with NSCLC
- FDG-PET
- Standard 60 Gy vs up to 30 Gy dose escalation
- Selective vs non-selective dose escalation

☞ DPBN >≈ NSDE > 60 Gy

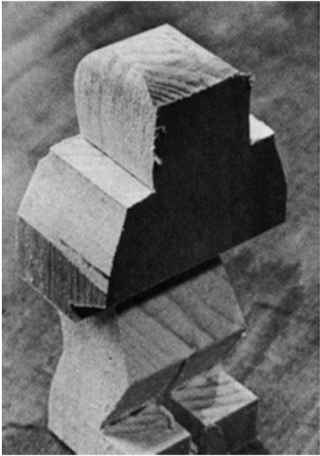# Some progresses…

"1-D Imaging"

< 1950

2-D Imaging

≈ 1960

3-D Imaging

≈ 1990

Multimodality Imaging

≈ 2000

Molecular Imaging

≈ 2010

Synthetic Images

> 2023

Roma, Oct. 2023

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

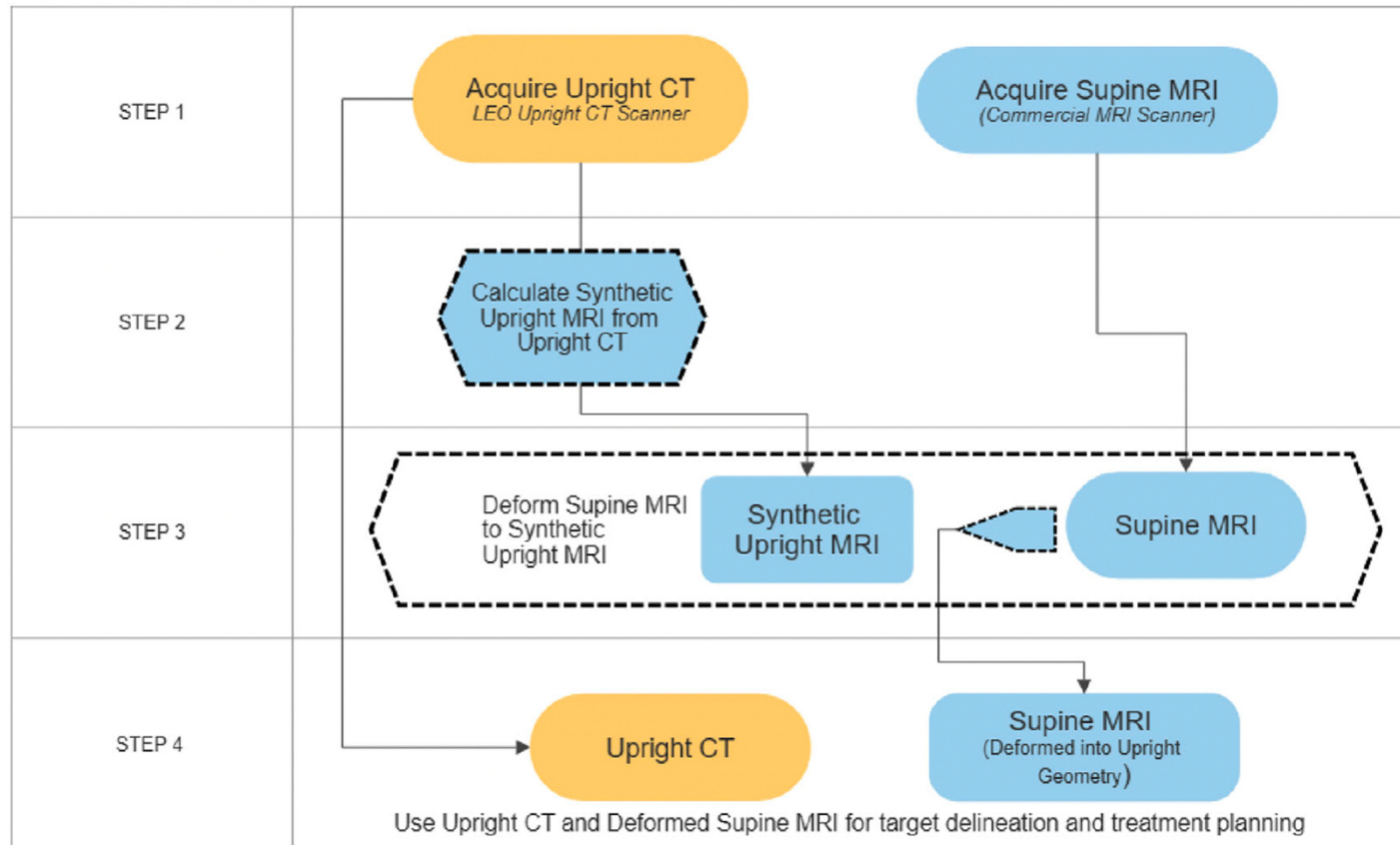# Synthetic images
What is what?

CT or sCT?
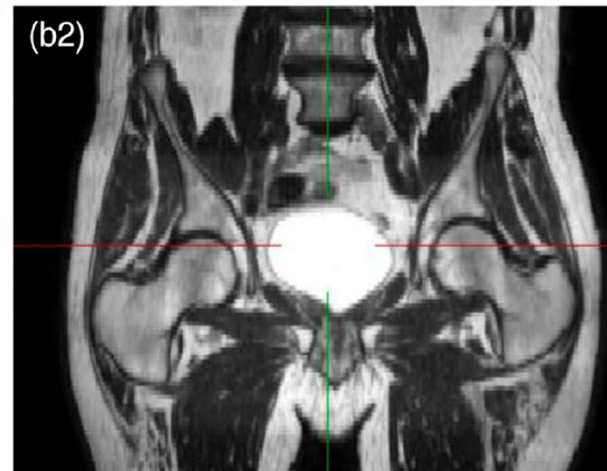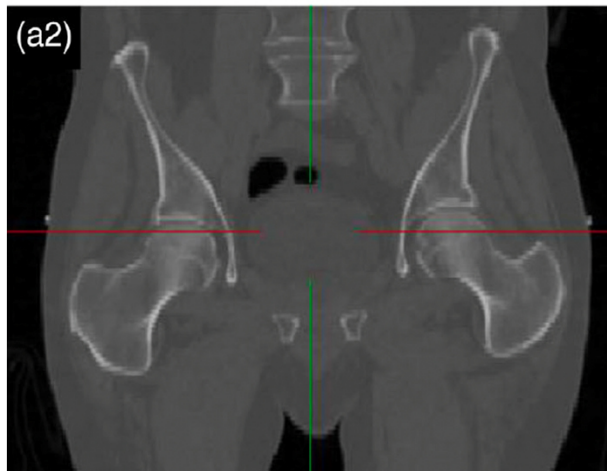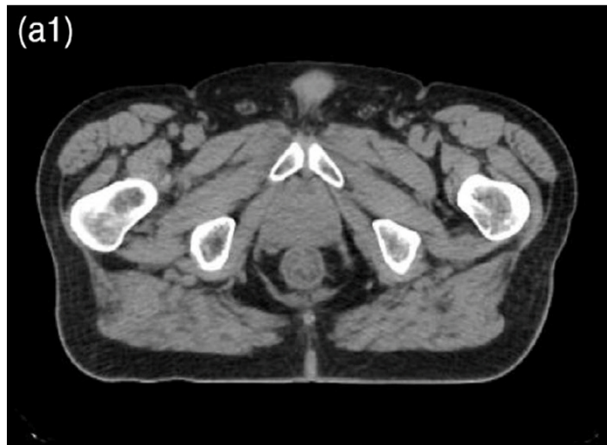
MRI or sMRI?

Synthetic images
From supine MRI to vertical MRI for up-right treatment
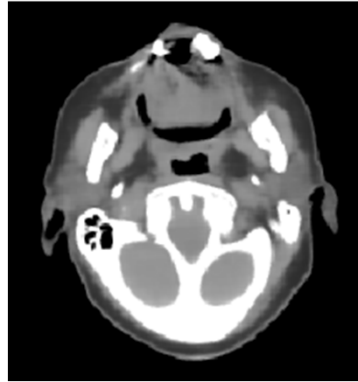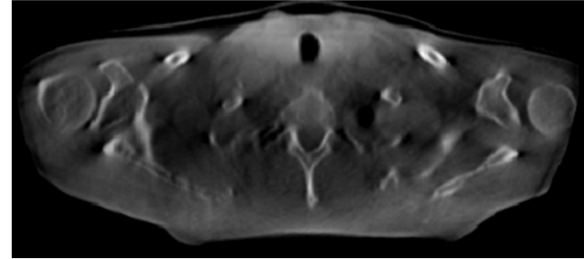
Schreuder et al, J Appl Clin Med Phys, 2023

CBCT   Synthetic CT   CBCT   Synthetic CT
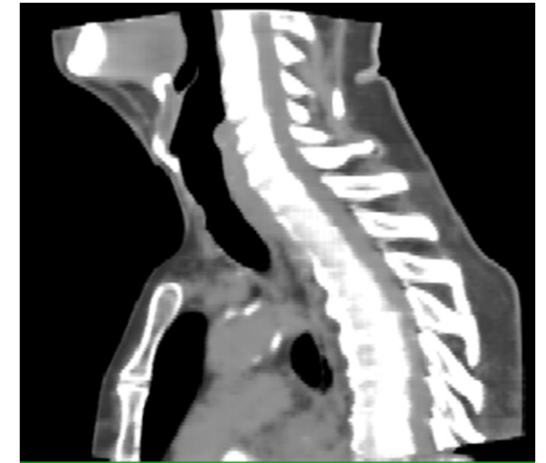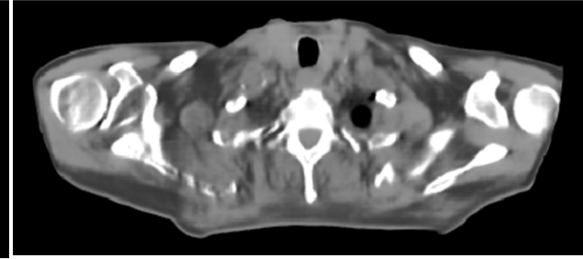
Roma, Oct. 2023

Some progresses…
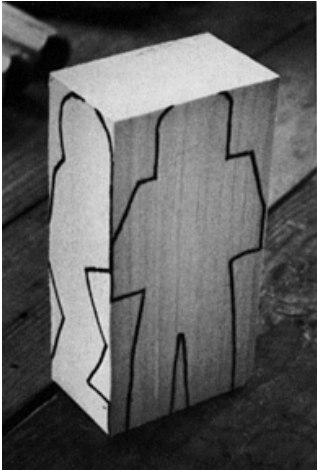
"1-D treatment"

< 1950

2-D treatment

≈ 1960

3-D treatment

≈ 1990

IMRT/VMAT

≈ 2000

Dose Painting

≈ 2010

Dose calculation on synthetic images

> 2023

Courtesy of John Schreiner, Kingston Regional Cancer Centre, Ontario

Dose generation on synthetic-CT from CBCT

- Retrospective study performed on 19 primary prostate cancer patients (10 Varian CBCTs and 9 Elekta CBCTs)
- Planning CT warped to the daily CBCT to eliminate changes due to positioning or organs movements
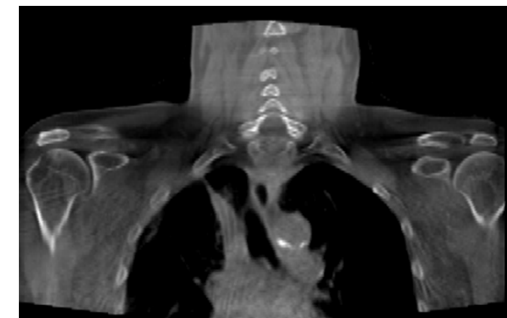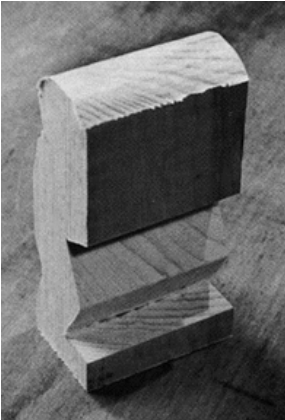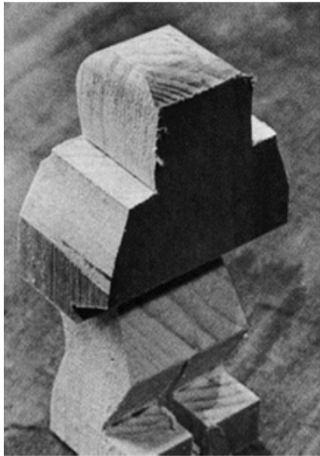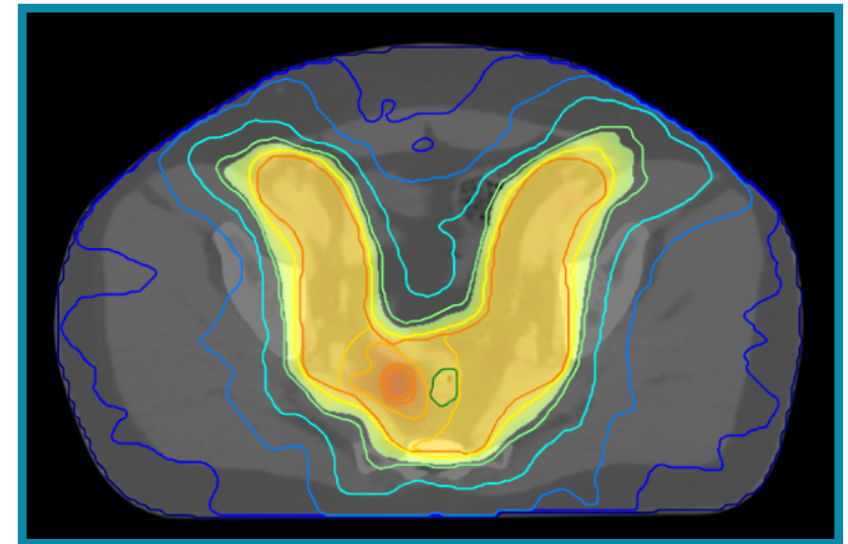- Treatment plans optimized on the planning-CT with a clinical TPS
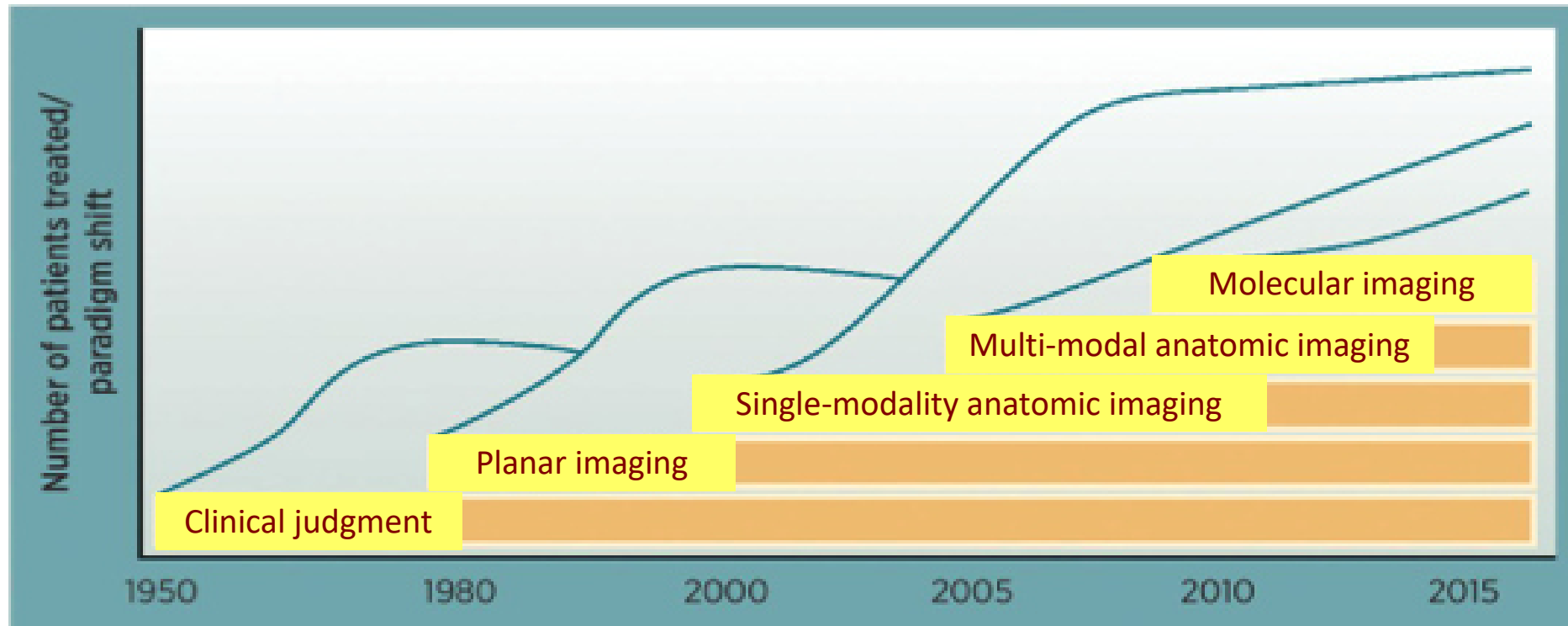- Dose recalculted on the planning-CT and synthetic-CT of the same patient

	DVH parameters	Median relative dose difference (%)	Mean relative dose difference (%)	Min relative dose difference (%)	Max relative dose difference (%)
PTV	Dmean	0,170	0,212	0,007	0,658
	Dmax	0,199	0,327	0,004	1,322
	D98	0,149	0,181	0,005	0,501
	D95	0,160	0,188	0,002	0,540
	D50	0,180	0,234	0,011	0,896
	D5	0,164	0,234	0,004	1,340
	D2	0,170	0,241	0,001	1,359

Median and mean (min and max) relative dose difference for PTV between planning-CT and synthetic-CT from CBCT

Synthetic-CT from CBCT with isodose and dose map

THERAPANACEA
Reinventing cancer care through AI

CENTRE DE LUTTE CONTRE LE CANCER
LEON BERARD

Roma, Oct. 2023

Courtesy of N. Paragios, 2023

# Imaging evolution for improved Target Volume & normal anatomy definition

Roma, Oct. 2023

Evolution of Radiotherapy delivery for improved dose distribution and patient outcome
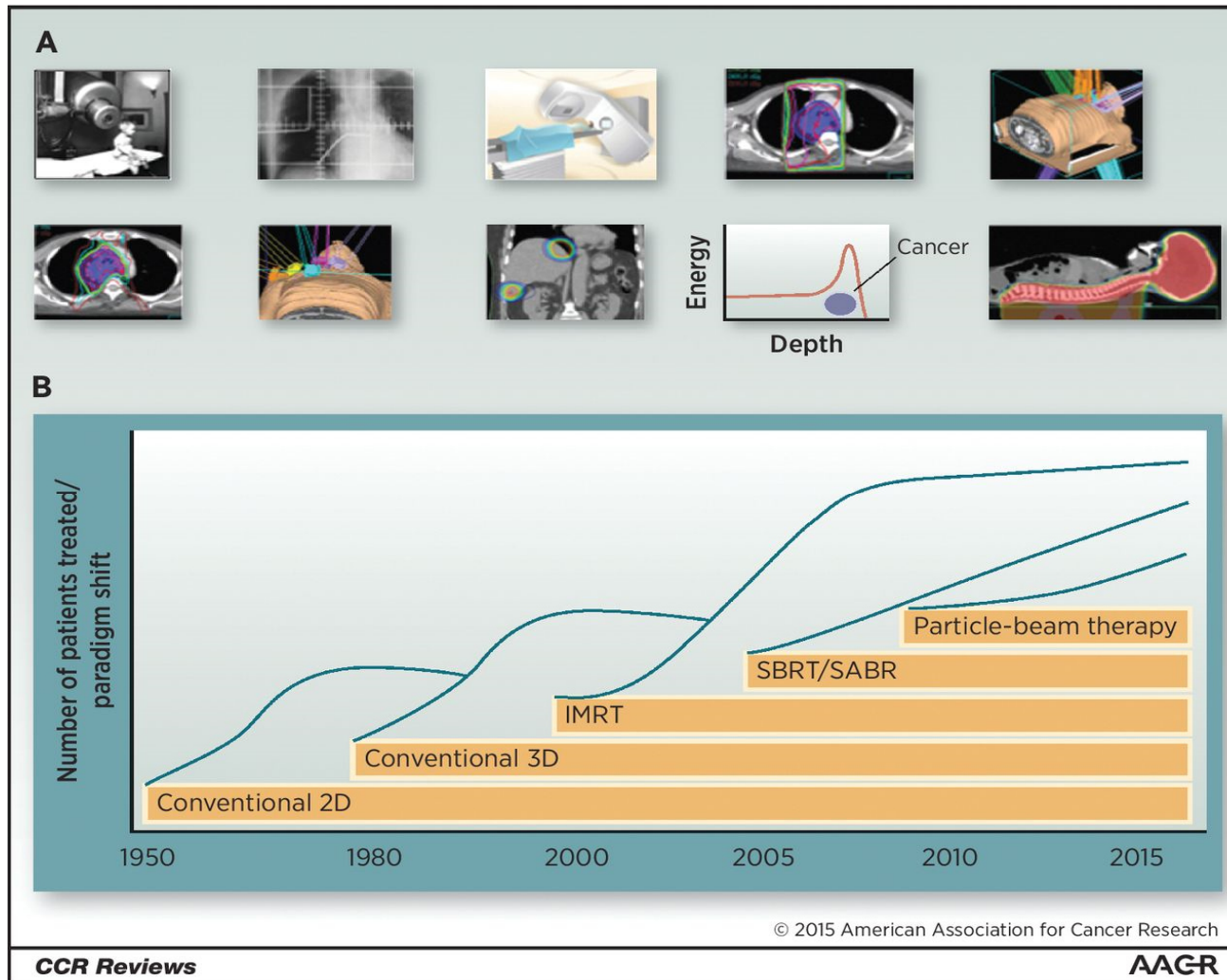
From medical art …

Discovered in 1895 and immediately used for the treatment of cancer… Why so quickly? Surgery was the only option but it was not armless…

CENTRE DE LUTTE CONTRE LE CANCER
LEON BERARD
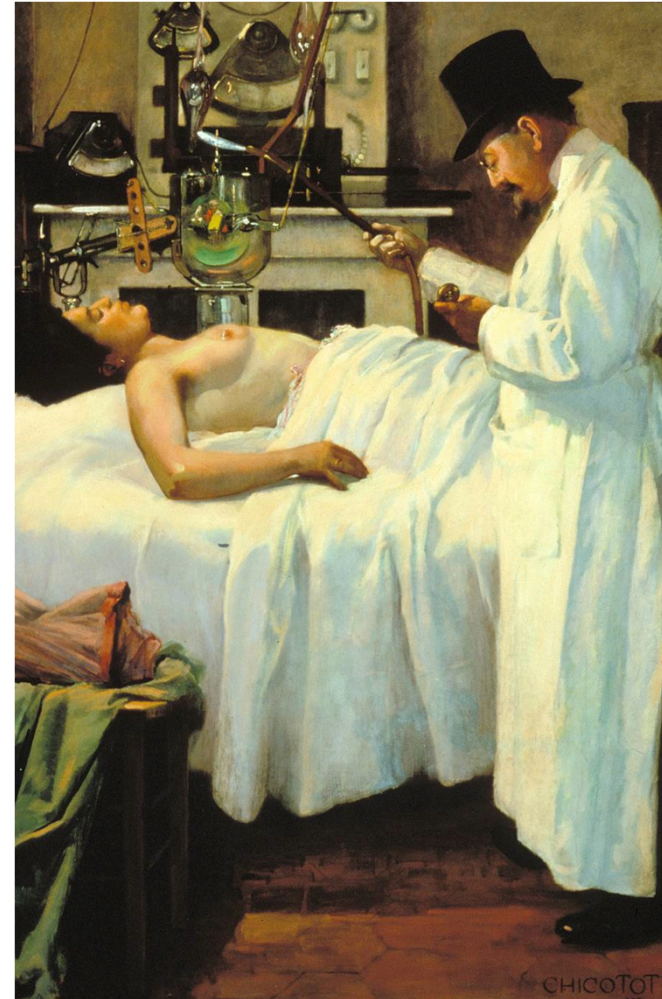
… to personalized Radiation Oncology.

"Here's my omics ..."

One patient …

One disease …

One treatment …

Roma, Oct. 2023

CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Nature, 2000