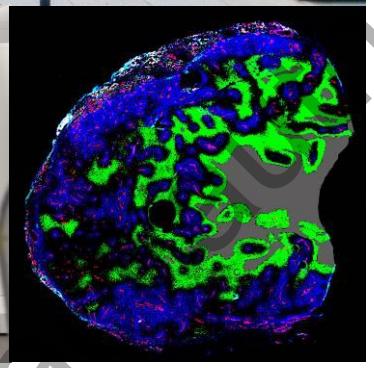


Evaluation and further development of particle therapy in Europe

Michael Baumann

Department of Radiation Oncology,
Medical Faculty and Univ. Hospital, TU Dresden

OncoRay – Natl. Center for Radiation Research in Oncology, Dresden

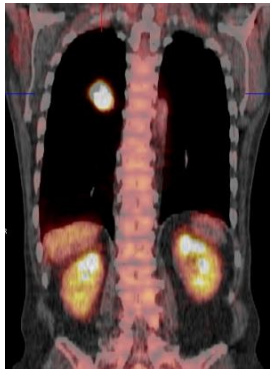
Institute of Radiation Oncology,
HZDR Dresden

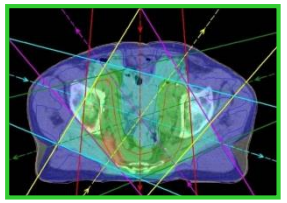
German Cancer Consortium (DKTK),
Partnersite Dresden

National Center for Tumor Disease (NCT),
Partnersite Dresden

Cancer

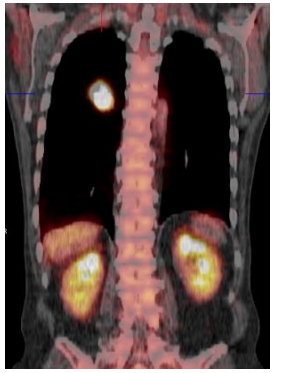
- > 2m new cases/a in Europe
  (w/o small skin cancers)
- Incidence: 1 / 2-3 citizens
- Death: 1 / 4-5 citizens
  (2nd most frequent cause of death)
- Steeply increasing in low income countries
- Surgery, radiotherapy, systemic therapies
  (increasingly combinations, cancer centers)
- Cure rates approximately 50%

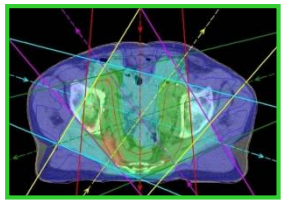




Radiation Oncology

- 50% of all cancer patients
- Highly individualized treatment
- 50% of cures – radiotherapy sole treatment or major component
- Organ- and function sparing, well tolerable
- More than 4m long term survivors in Europe
- Favorable cost/benefit





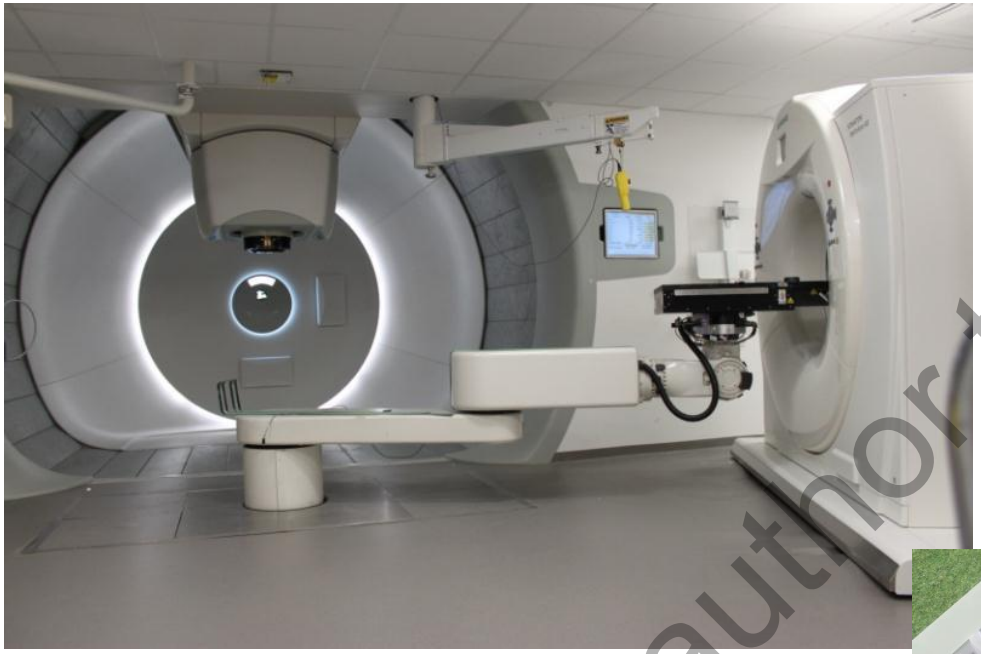
State of the art

Image guided, conformal (IMRT), photon therapy (Linacs)

- 35% local recurrence
- Preventable distant metastases
- Large volumes irradiated
- Early, late and very late normal tissue damage

- Potential of particle therapy
- Real time adaptation (motion, changes)
- (Biological individualization)

Particle therapy

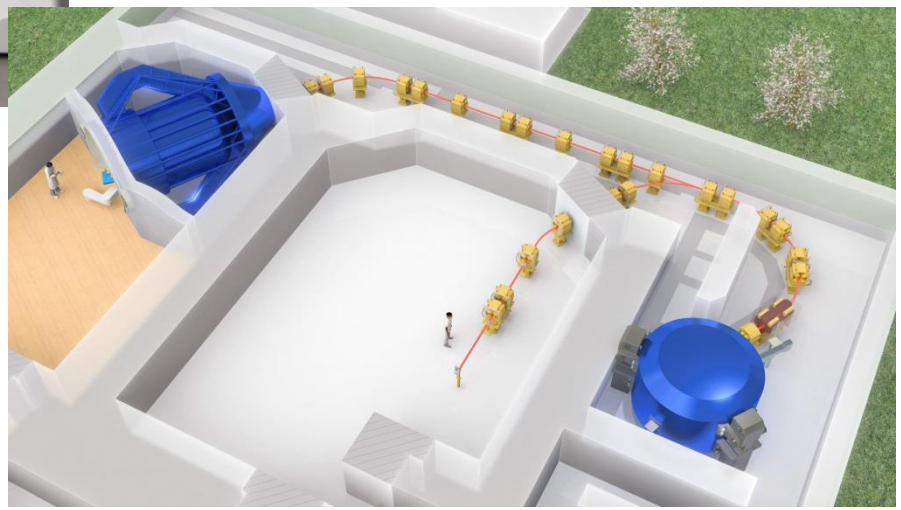


50 units worldwide

P, C

>110.000 pts treated

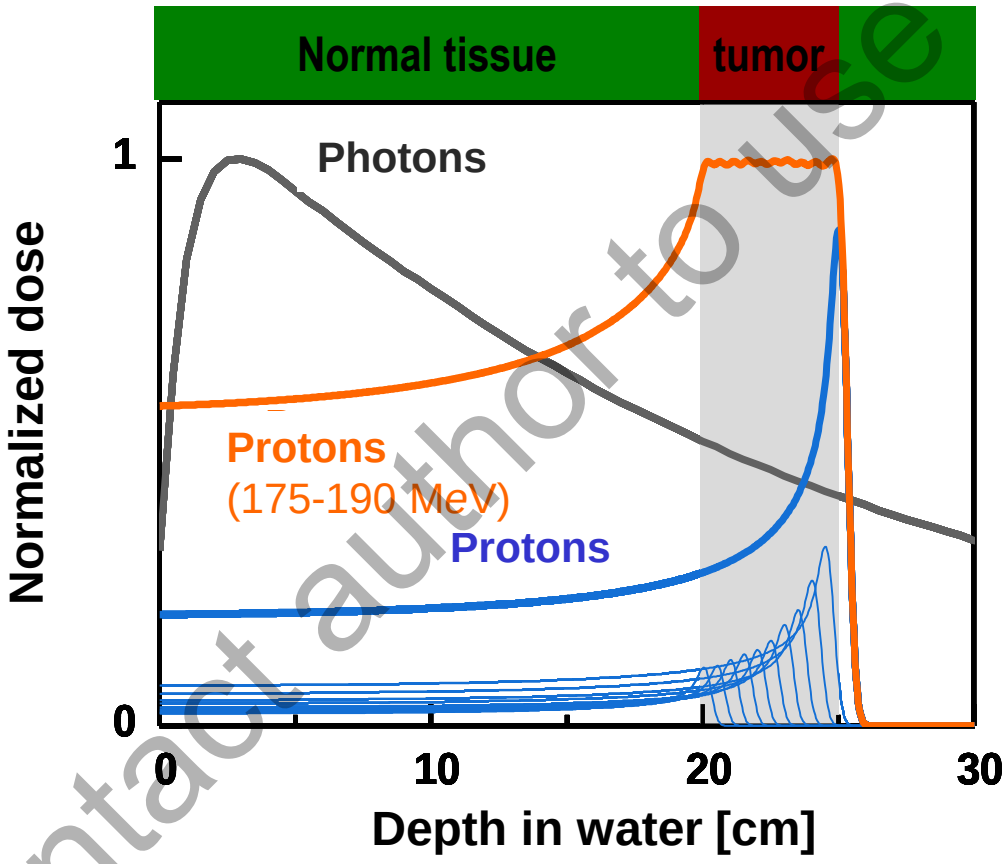
soon >15.000 pts/a Europe



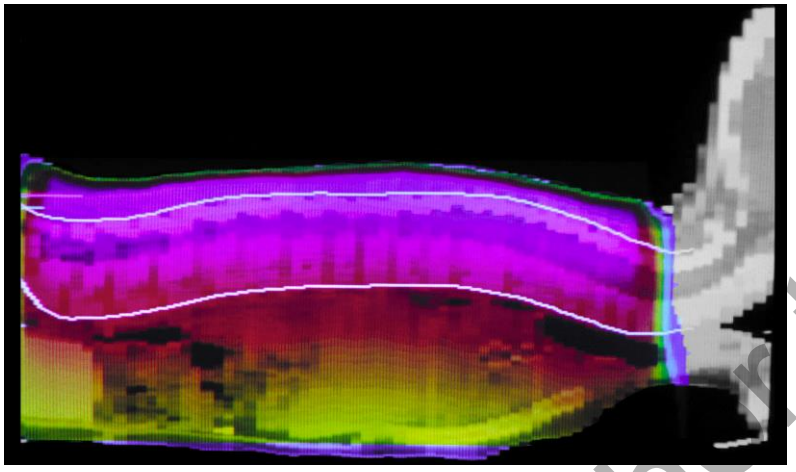
Universitäts Protonen Therapie Dresden

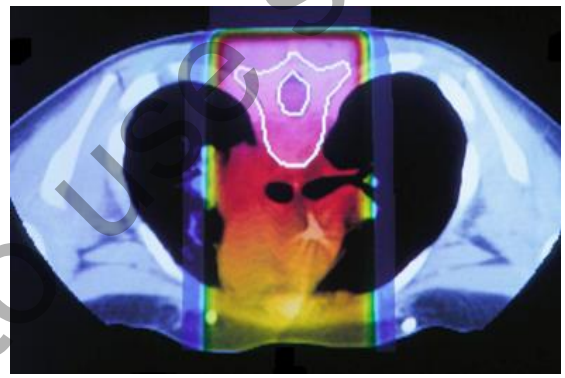
Klinik für Strahlentherapie OncoRay

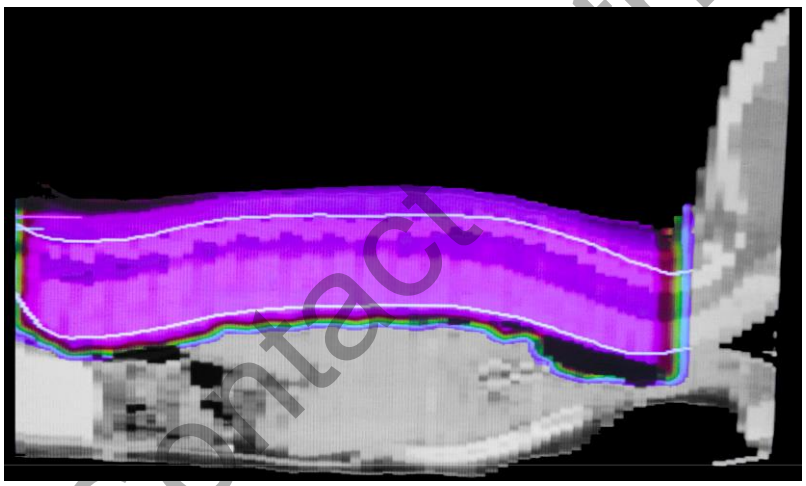
Physical basis

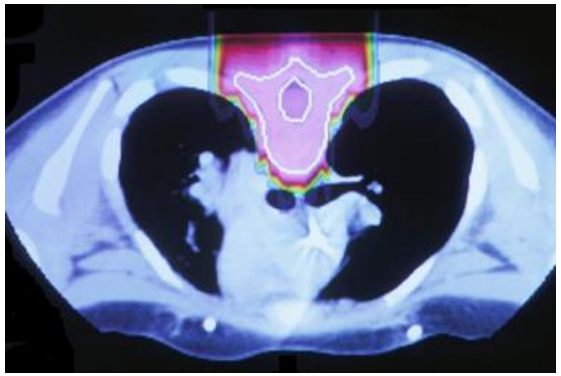


Potential of particle therapy



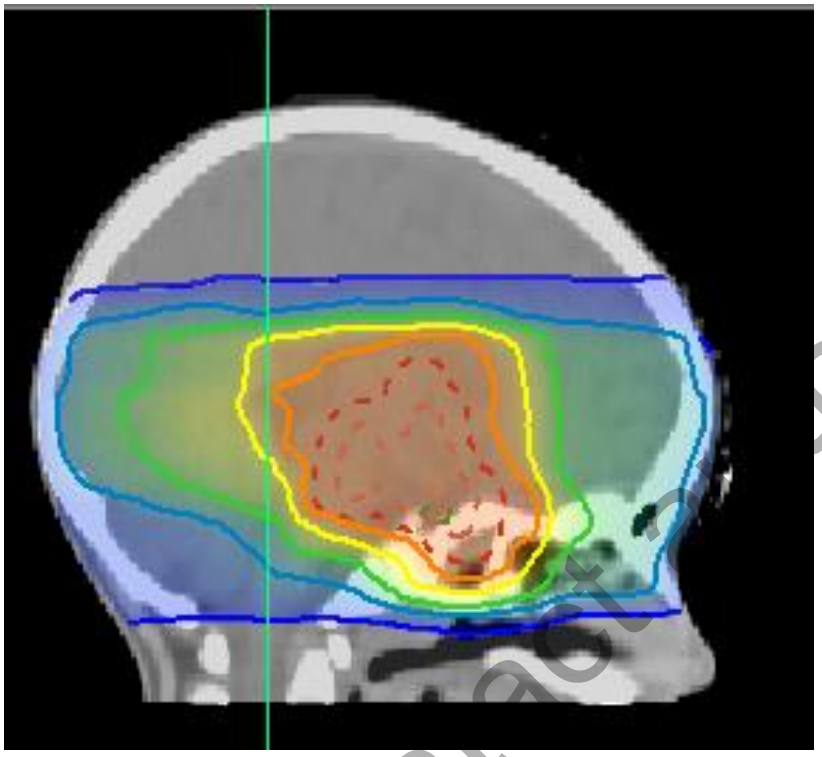






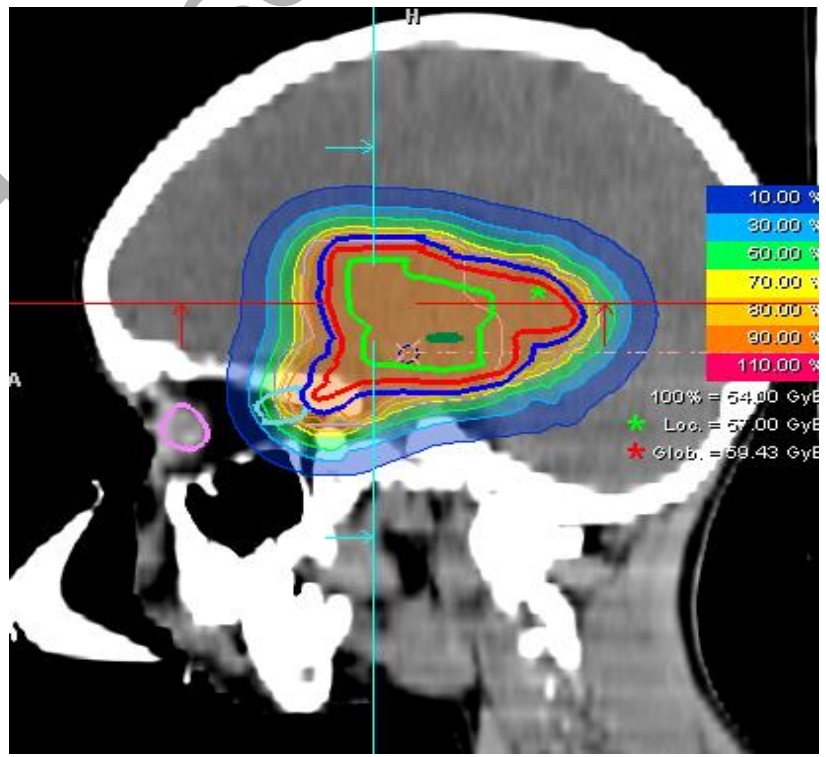
Potential of particle therapy

Photon-IMRT



Universitätsklinikum Dresden

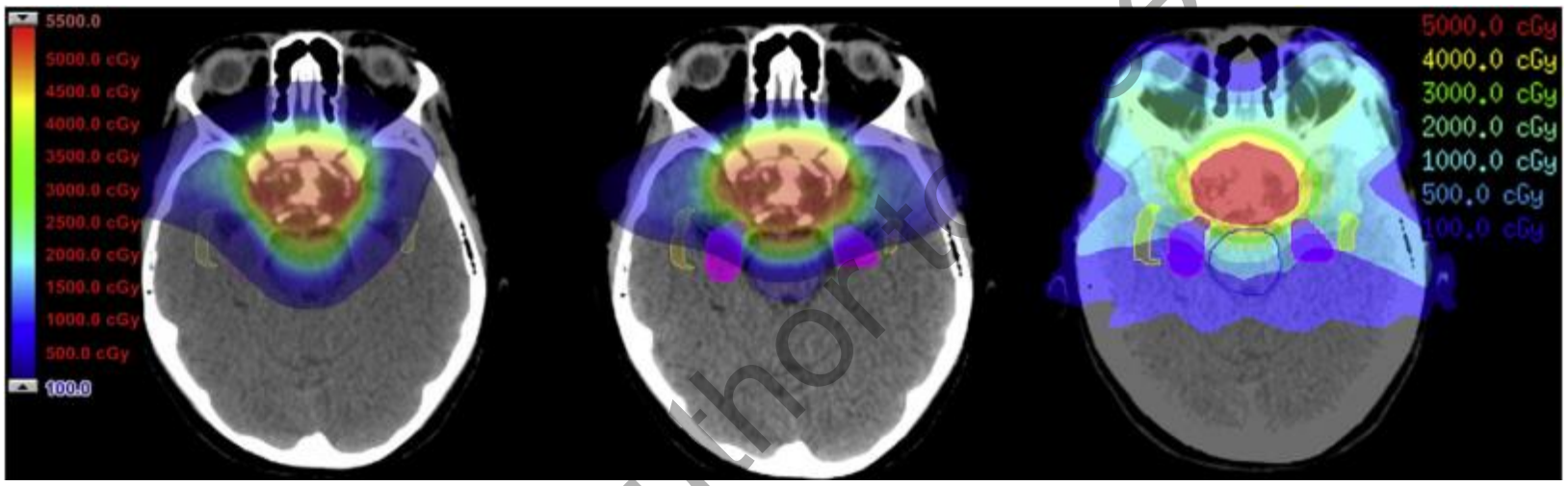
Protons

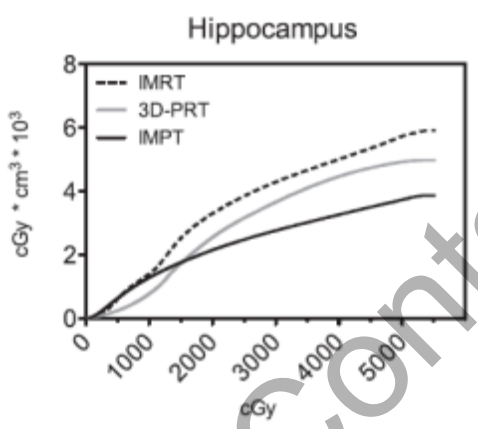


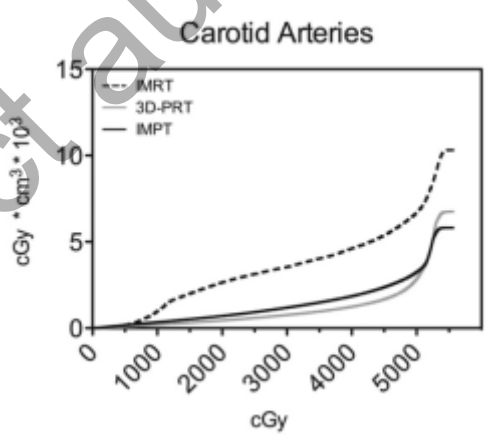
HIT, Heidelberg

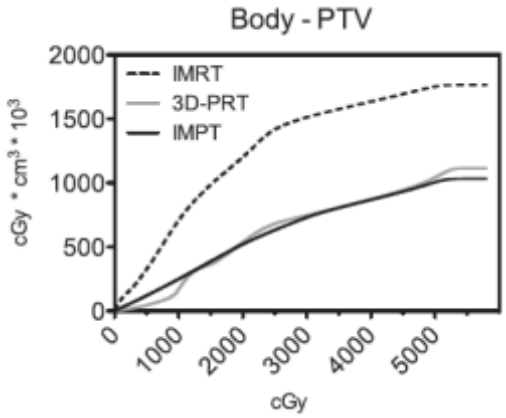
Potential of proton therapy

3D-PRT IMPT IMRT



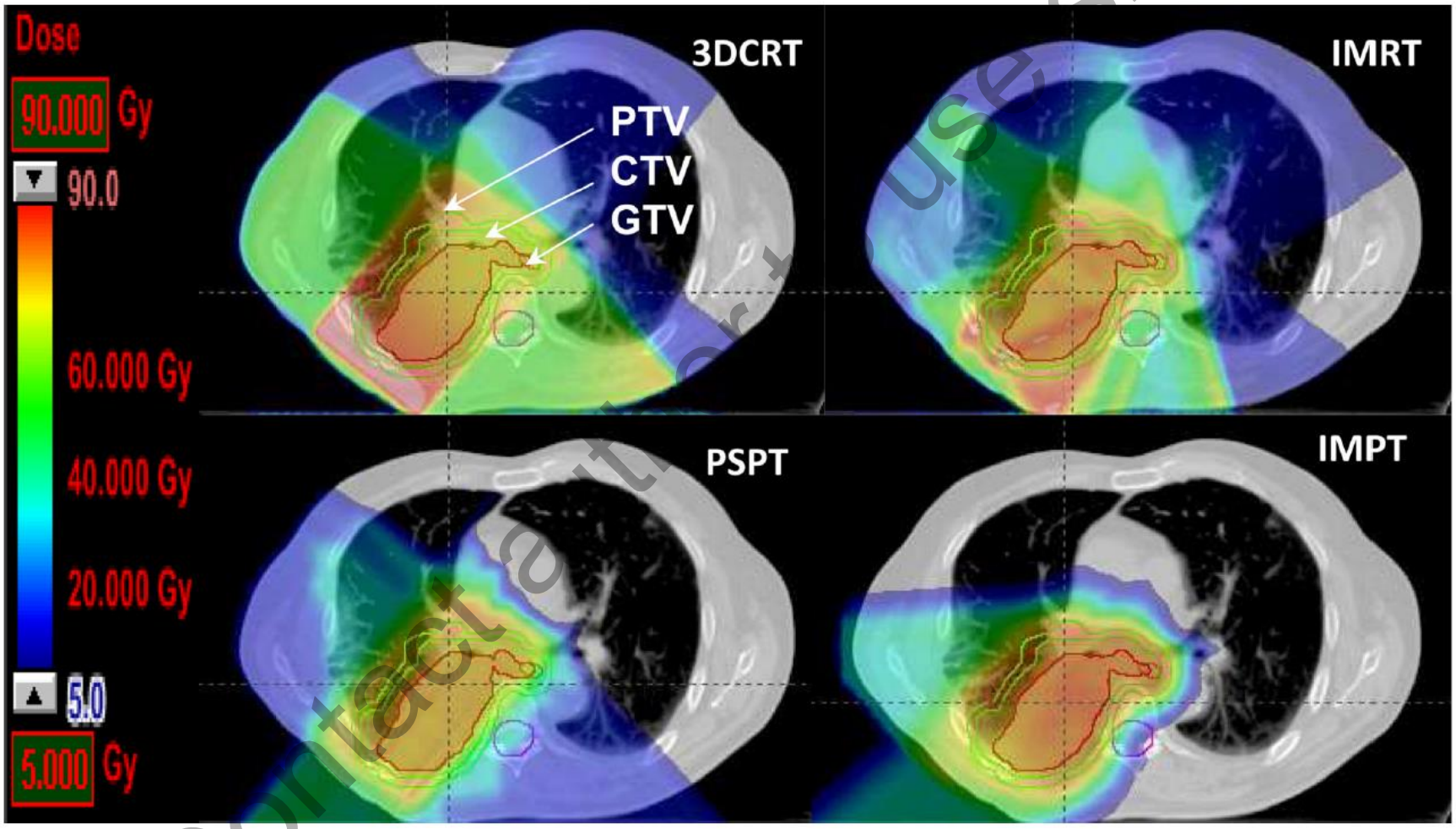






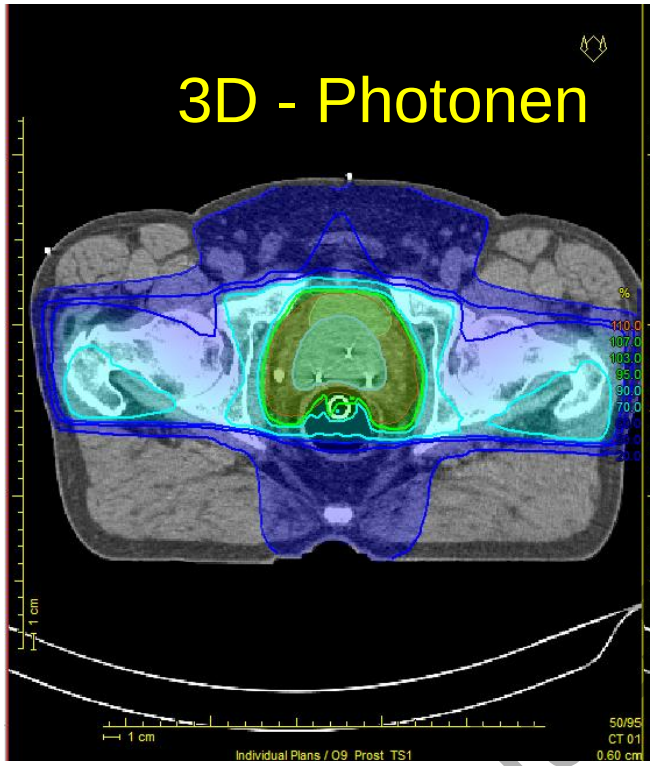
Boehling et al., IJROBP 82, 643-52, 2012

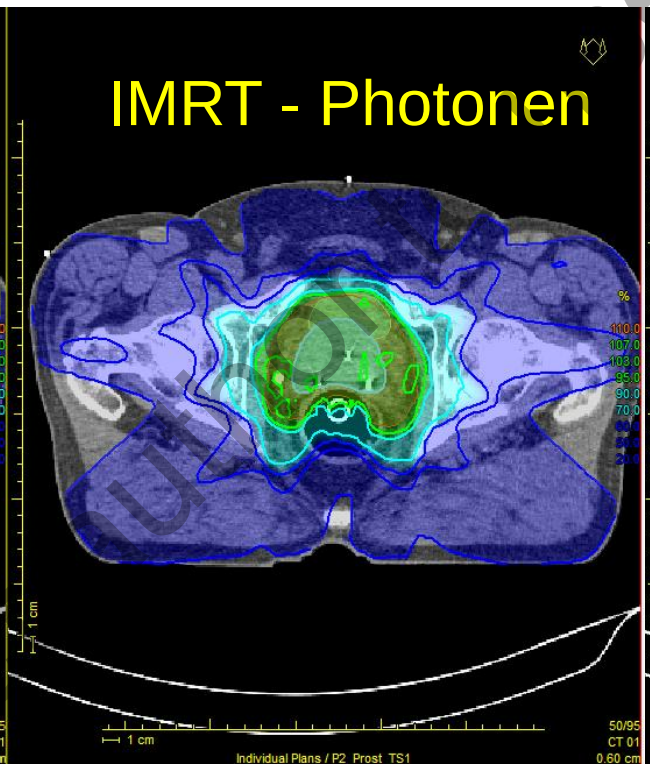
Potential of particle therapy

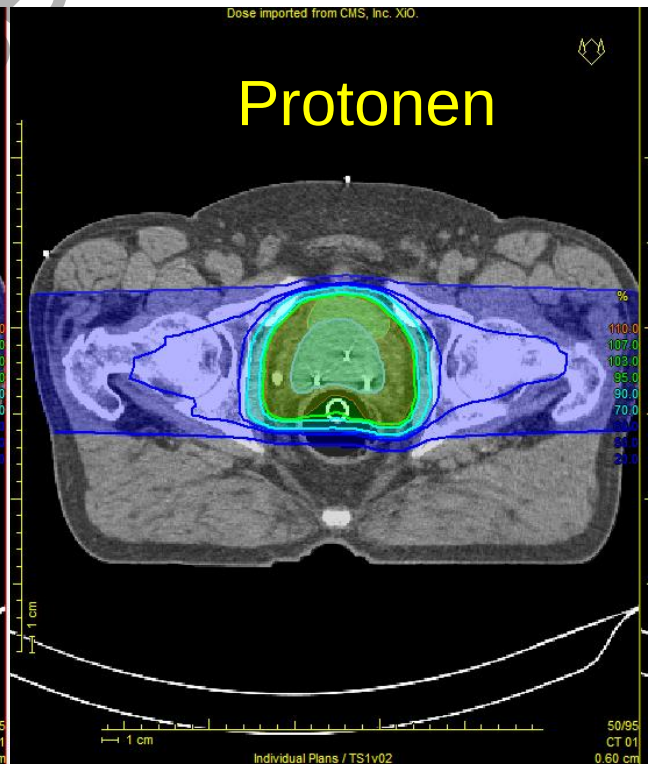


Chang et al., *Semin Radiat Oncol 20(3)*: 171-177, 2010

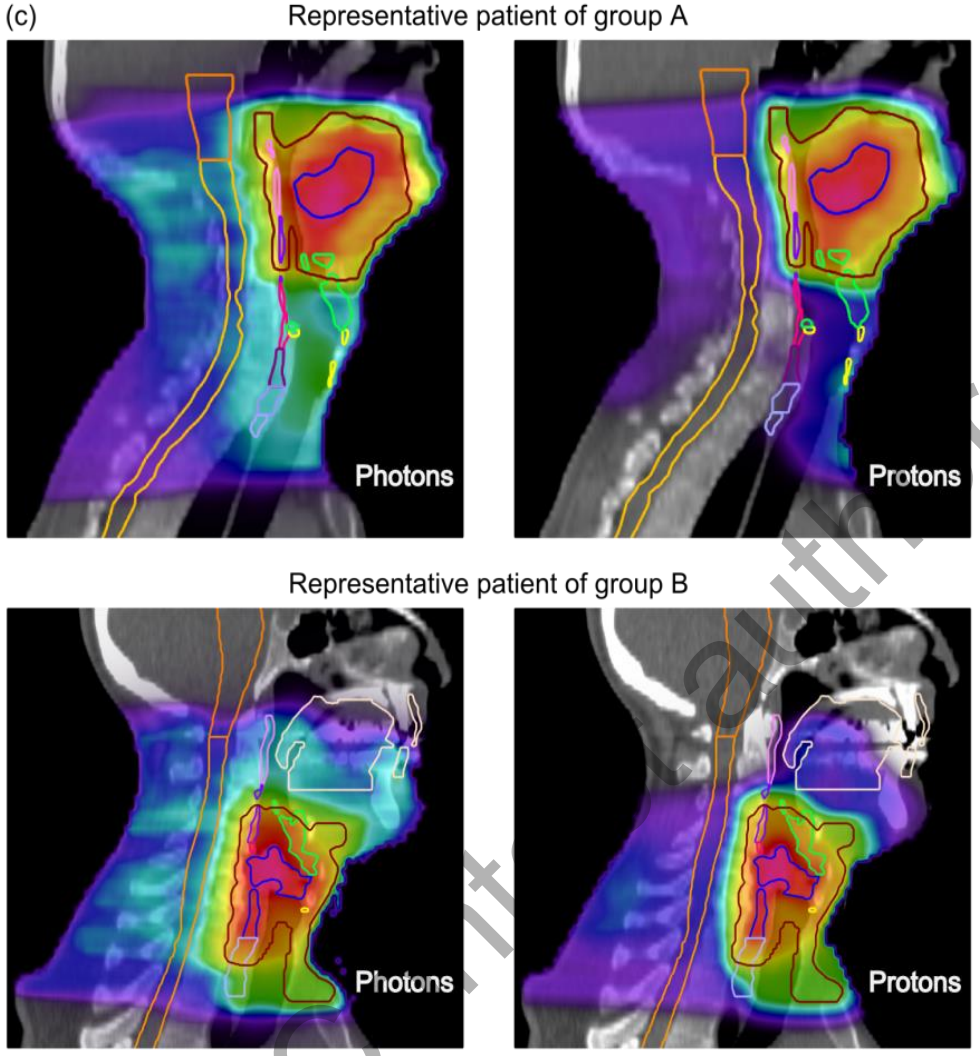
Potential of particle therapy

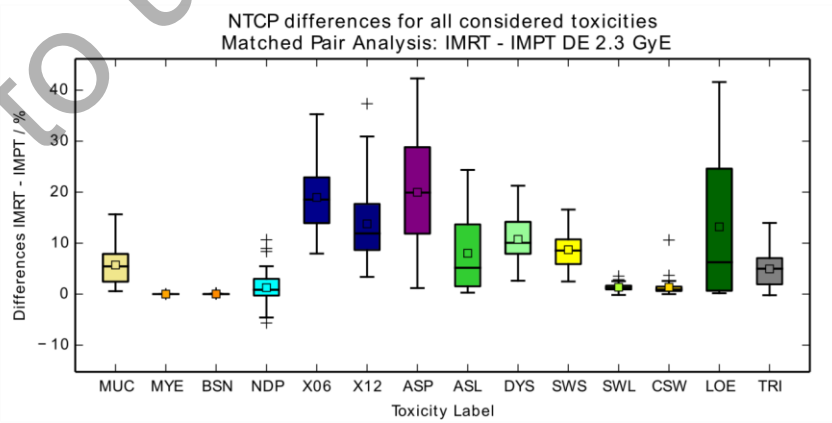






Potential of particle therapy

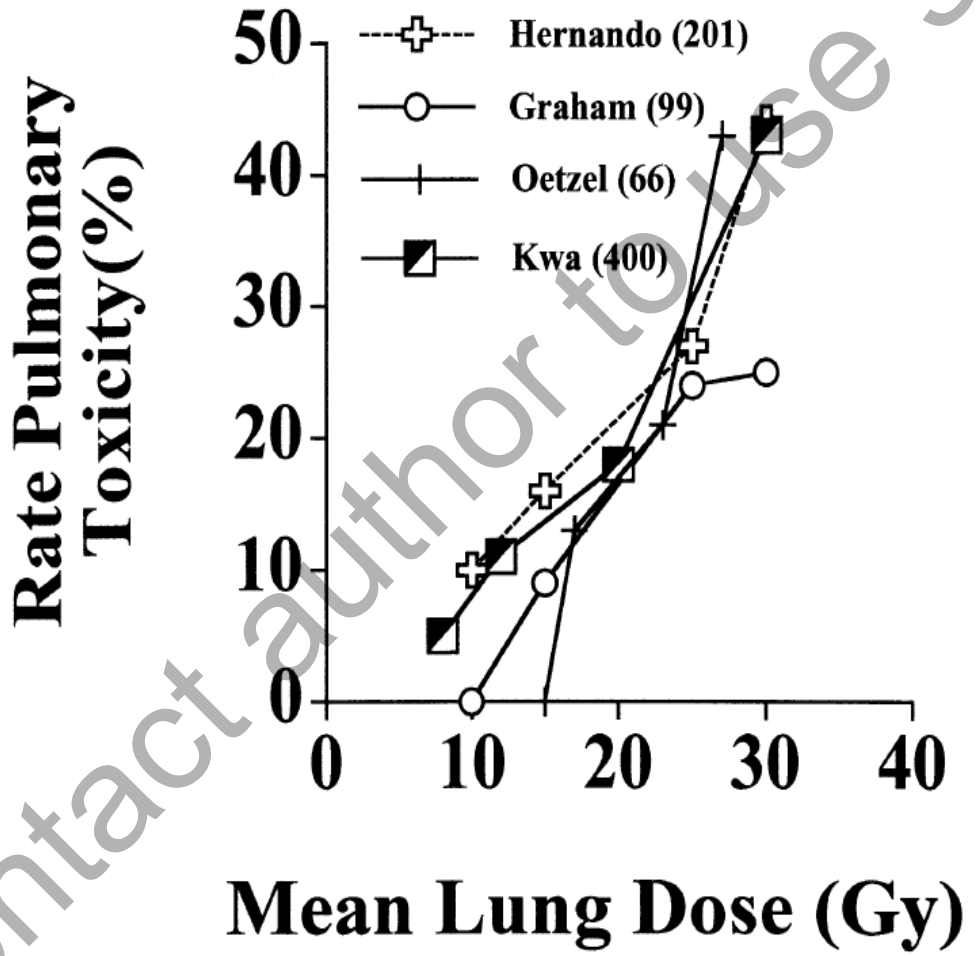




MUC: Oral mucositis
MYE: Myelopathy
BSN: Brain stem necrosis
NDP: Nerve damage of brachial plaxus
X06: Xerostomia after 6 months
X12: Xerostomia after 12 months
ASP: Aspiration based on pharyngeal constrictor muscles
ASL: Aspiration based on larynx
DYS: Physician-rated swallowing dysfunction
SWS: Patient-rated problems swallowing solid food
SWL: Patient-rated problems swallowing liquids
CSW: Patient-rated choking when swallowing
LOE: Laryngeal oedema
TRI: Trismus

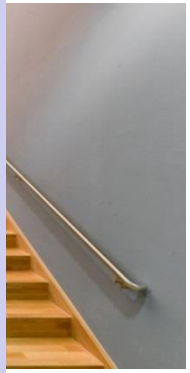
Jakobi et al., IJROBP 2015

Volume and NTCP



Potential of particle therapy to explore

- We do not know much about the impact of low and intermediate doses and
- dose volume relationship on normal tissue reactions
- ...nor on the interactions of low and high doses



Data needed

- Patient cohorts
- Clin
- Ima
- Rad
- Tre
- (Sp
- Biological data/ materials
- Economic data

Dose Plan Data Banks
(with network compatibilty)

Modell-based approach

Radiotherapy and Oncology 107 (2013) 267–273

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

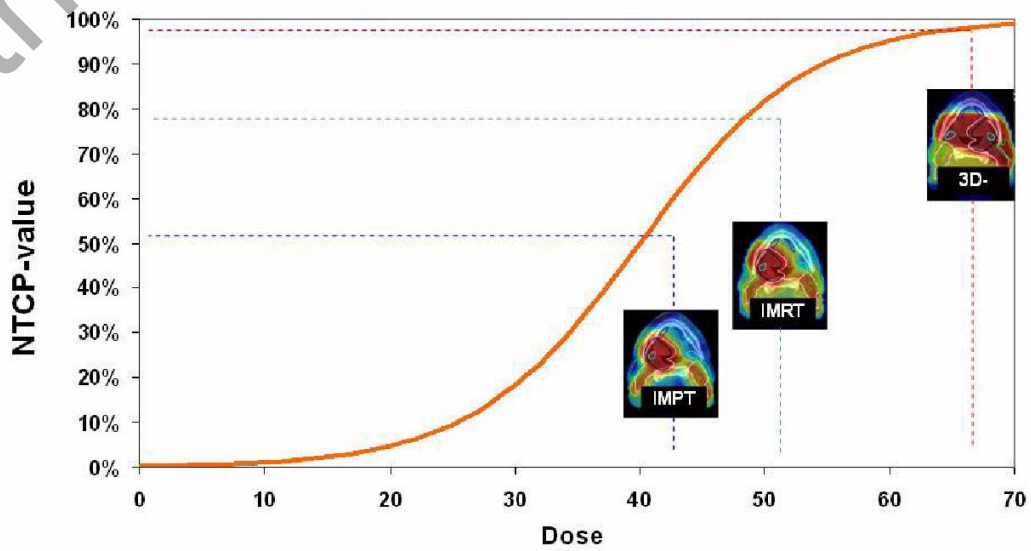
journal homepage: www.thegreenjournal.com

Proton radiotherapy

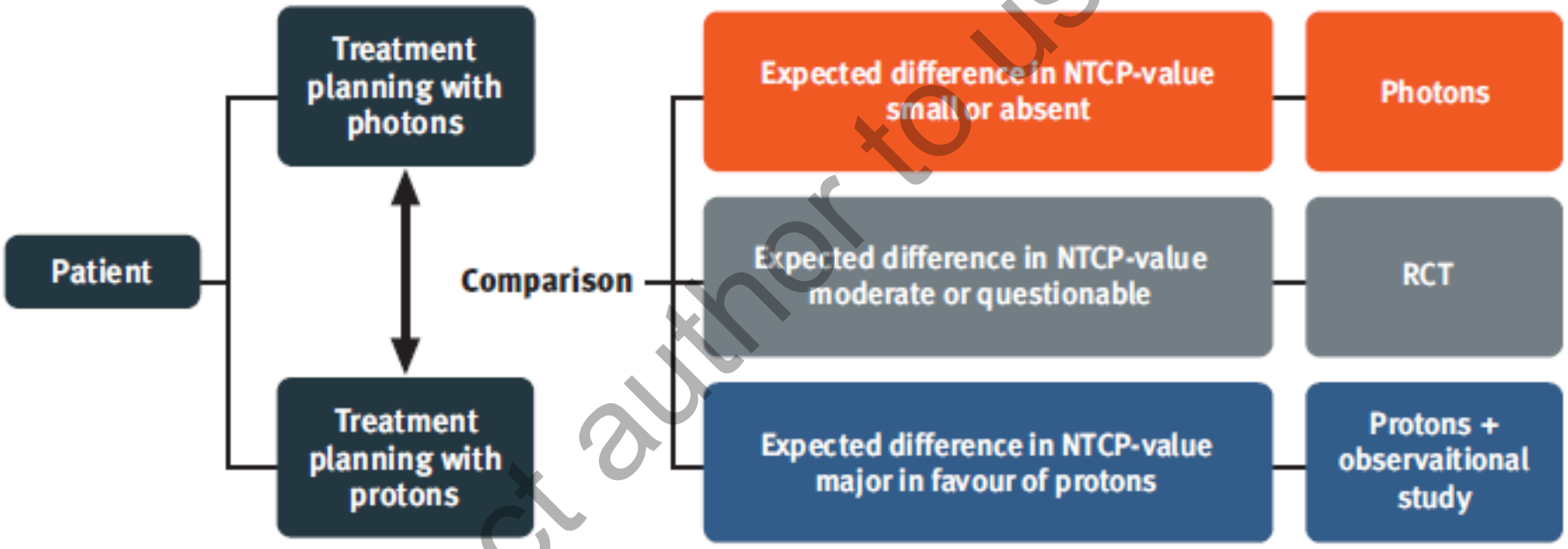
Selection of patients for radiotherapy with protons aiming at reduction of side effects: The model-based approach

Johannes A. Langendijk [a,*], Philippe Lambin [b], Dirk De Ruysscher [c], Joachim Widder [a], Mike Bos [d], Marcel Verheij [e]

[a] Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, The Ne
Research Institute GROW, University Hospital Maastricht, The Netherlands; [c] Department of Radiation Oncology
the Netherlands; [e] Department of Radiotherapy, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Ho

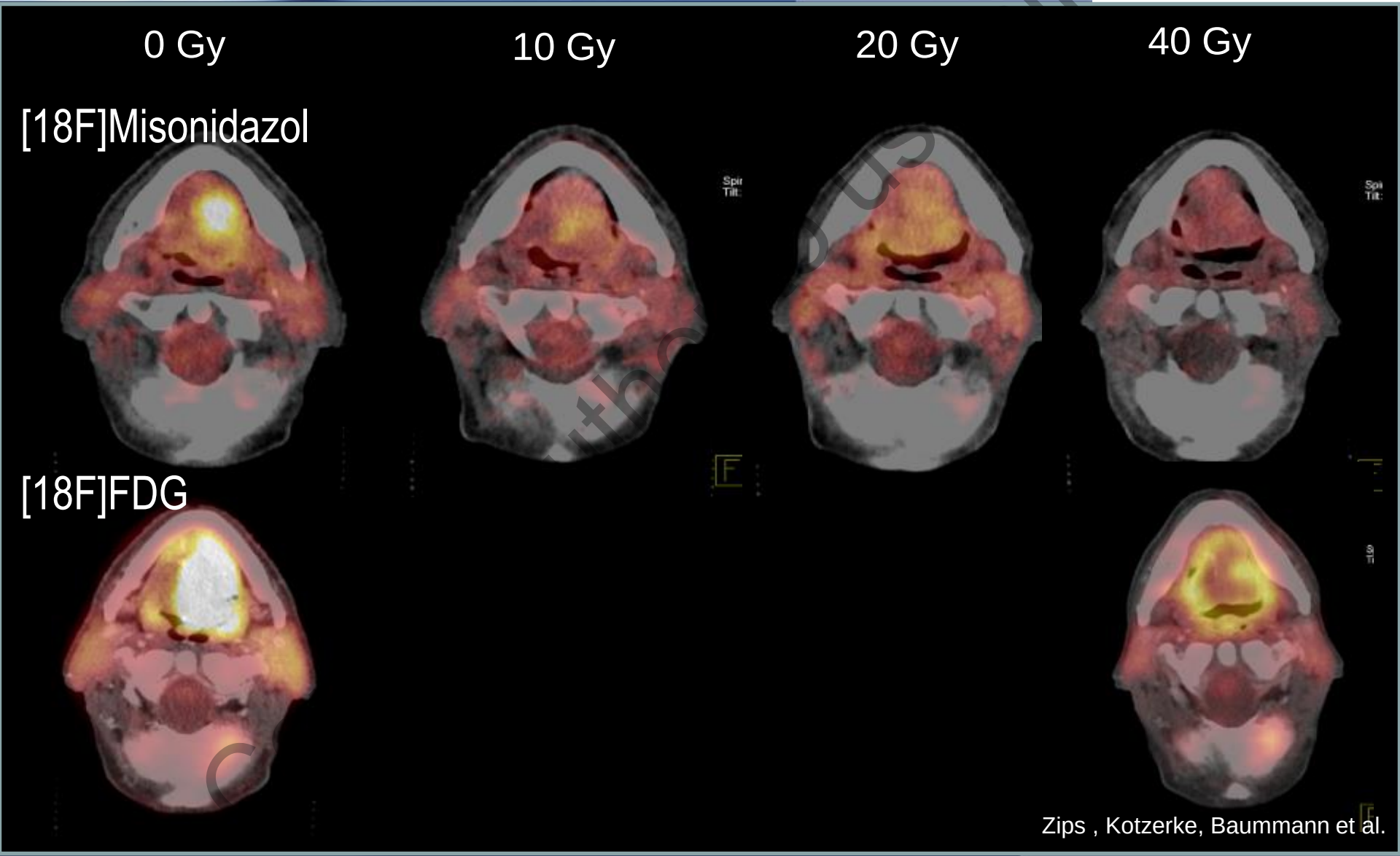


Modell-based approach: individual allocation



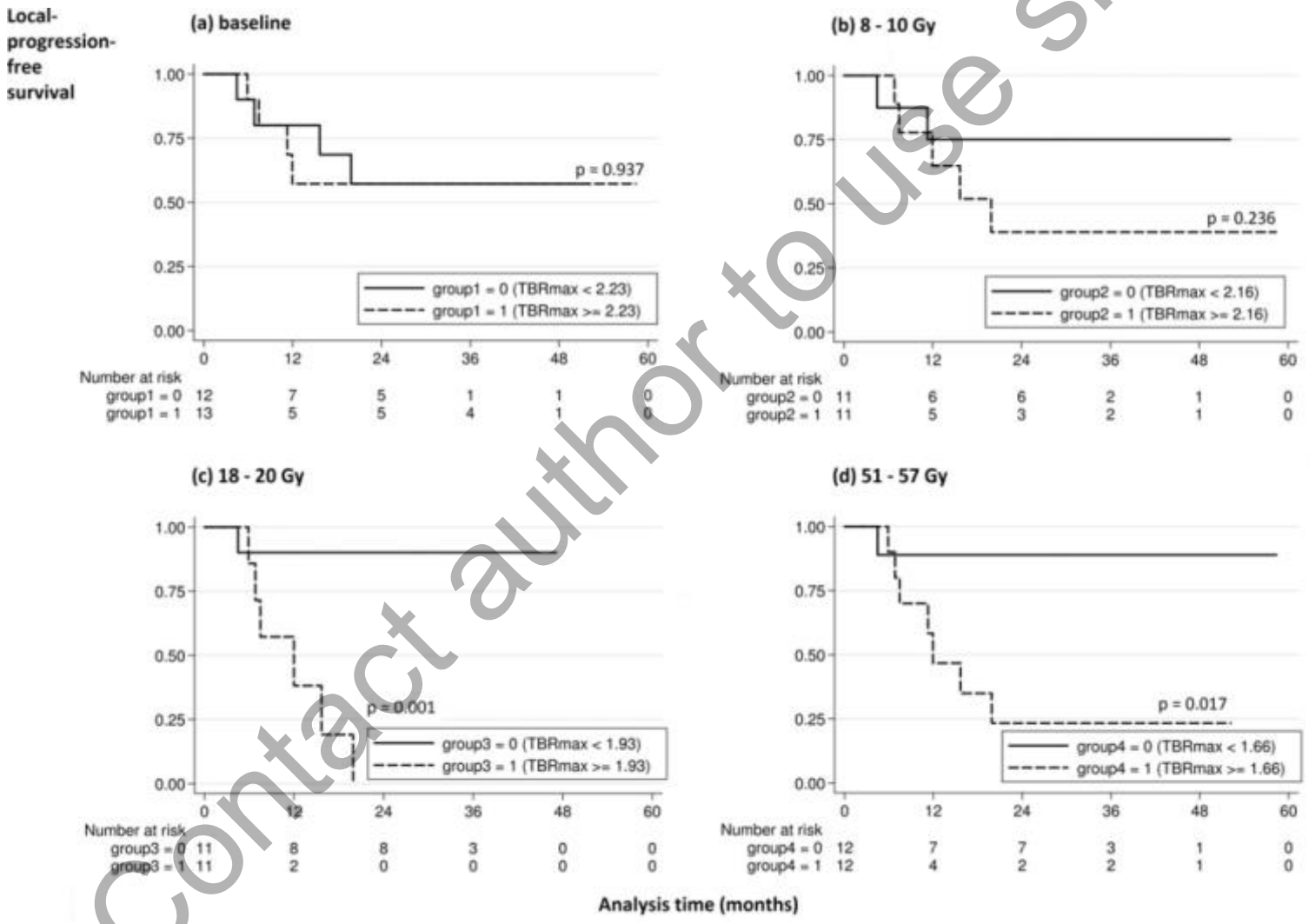
Danish and Dutch groups

Stratification



Zips , Kotzerke, Baummann et al.

Stratification



MOLECULAR STRATIFICATION BY HPV (RCT, POSTOP)

Contents lists available at ScienceDirect

Radiotherapy and Oncology

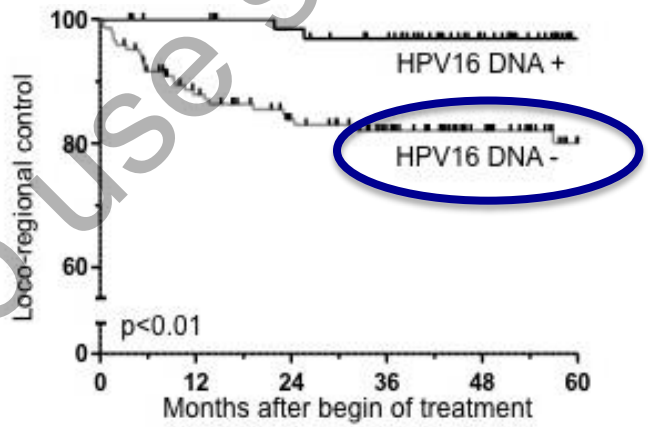
journal homepage: www.thegreenjournal.com

HPV in postoperative RT of oropharynx

HPV16 DNA status is a strong prognosticator of loco-regional control after postoperative radiochemotherapy of locally advanced oropharyngeal carcinoma: Results from a multicentre explorative study of the German Cancer Consortium Radiation Oncology Group (DKTK-ROG)

Fabian Lohaus [a,i,j,1], Annett Linge [a,i,j,1], Inge Tinhofer [b,k], Volker Budach [b,k], Eleni Gkika [c,l], Martin Stuschke [c,l], Panagiotis Balermpas [m], Claus Rödel [d,m], Melanie Avlar [e,n], Anca-Ligia Grosu [e,o], Amir Abdollahi [f,p,q,r], Jürgen Debus [f,p,q,s], Christine Bayer [g], Claus Belka [g,t], Steffi Pigorsch [g,u], Stephanie E. Combs [g,u], David Mönnich [h,v], Daniel Zips [h,v], Cläre von Neubeck [a,j], Gustavo B. Baretton [a,w,x], Steffen Löck [j], Howard D. Thames [z], Mechthild Krause [a,i,j,y], Michael Baumann [a,i,j,y,*], for the DKTK-ROG

post-op RCT

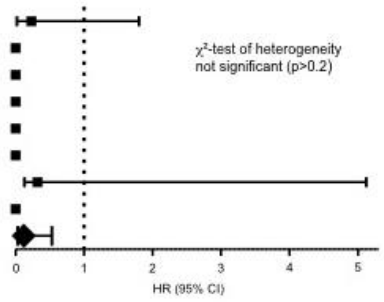


Patients at risk

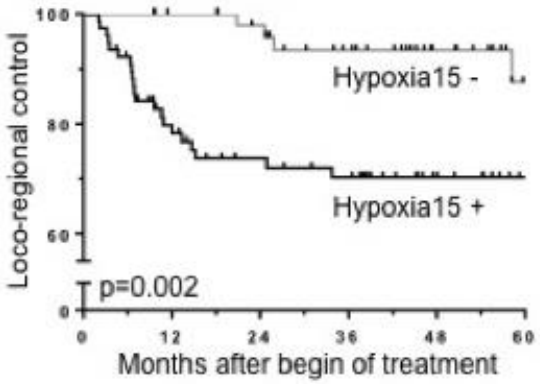
HPV16 DNA +	72	69	65	58	43	24
HPV16 DNA -	143	116	102	86	60	36

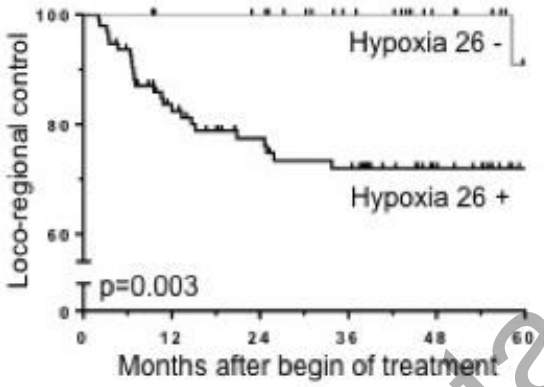
Treatment centre	Loco-regional control, HR (95% CI)		HPV16 DNA positive Events	HPV16 DNA positive Total	HPV16 DNA negative Events	HPV16 DNA negative Total
Centre 1	0.23	(0.02-1.80)	1	12	9	30
Centre 2	0	*	0	7	4	20
Centre 3	0	*	0	11	3	20
Centre 4	0	*	0	10	3	20
Centre 5	0	*	0	9	4	23
Centre 6	0	*	0	4	2	17
Centre 7	0.32	(0.02-5.12)	1	13	1	4
Centre 8	0	*	0	6	1	9
Overall	**0.13**	**(0.03-0.54)**	**2**	**72**	**27**	**143**

* No CI was calculated in case of no event in the HPV16 DNA positive group

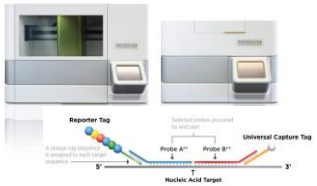


MOLECULAR STRATIFICATION OF HPV NEGATIVE HNSCC (RCT, POSTOP)





Nanostring Technology

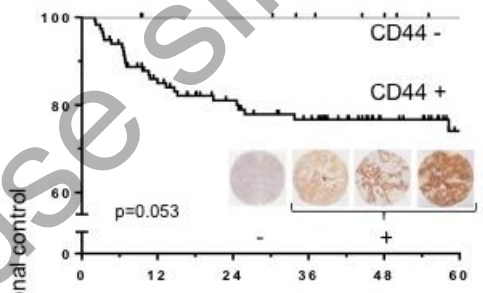


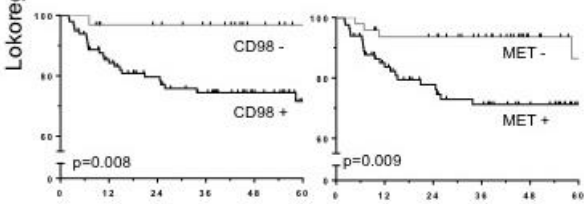
15 gene signature (Arhus)

26 gene signature (Manchester)

with local reccurrence

without local recurrence

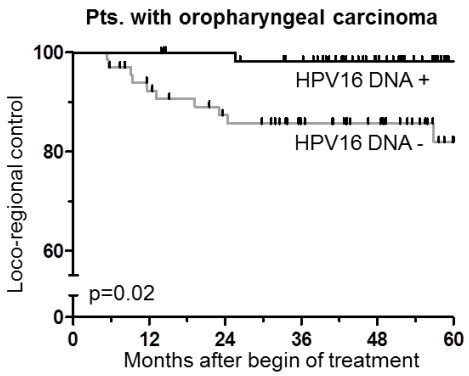


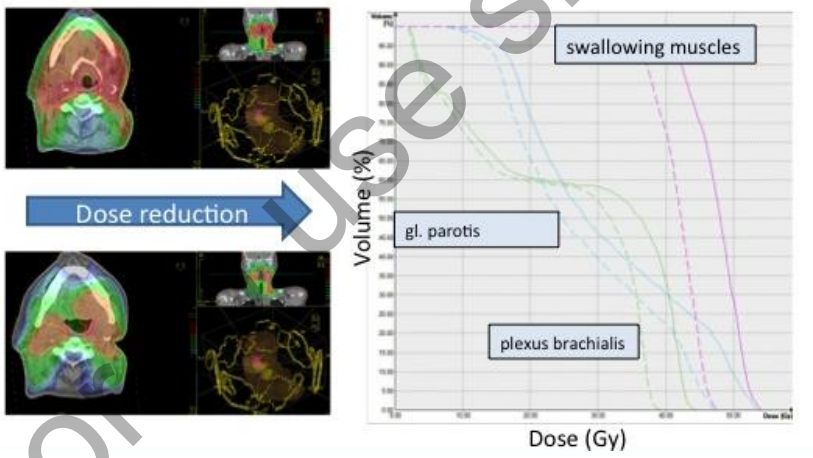


Months after start of treatment

		15-gene signature Hypoxia		26-gene signature Hypoxia	
		Low	High	Low	High
CD44	0	21	16	23	14
	1	48	96	42	102
		R=0.194	p=0.009	R=0.277	p<0.001
MET	0	52	42	59	35
	1	27	75	13	89
		R=0.294	p<0.001	R=0.518	p<0.001
CD98	0	44	33	55	22
	1	23	84	17	102
		R=0.276	p<0.001	R=0.579	p<0.001

INTERVENTIONAL TRIAL: DOSE DE-ESCALATION POST-OP HNSCC

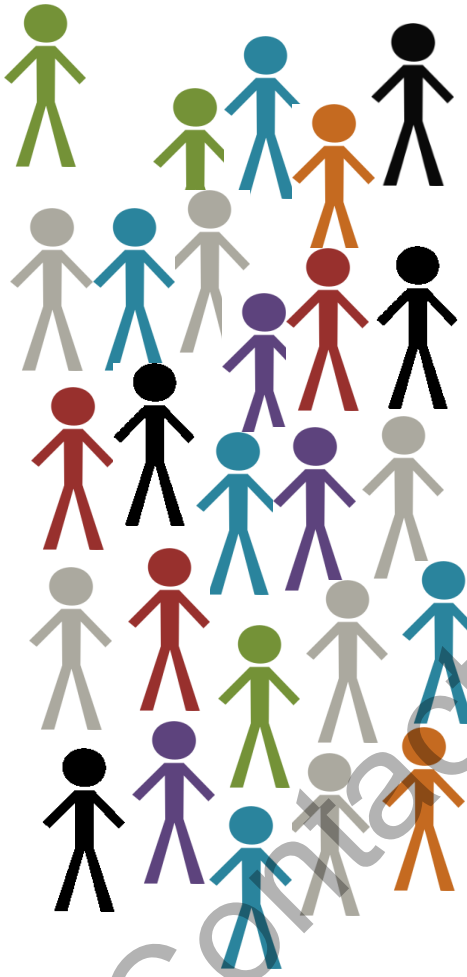


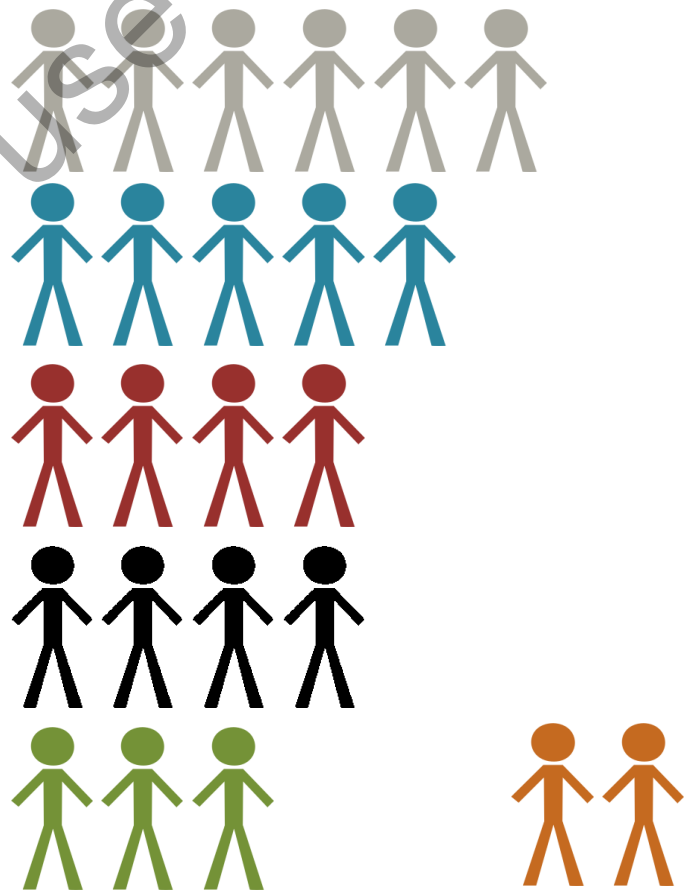


Dose level	Number of patients	RT-Dose (Gy)			Chemotherapy
		CTV A	CTV B	Σ	
1	30	44	16	60	Cisplatin 40mg BSA weekly i.v.
2*	30	40	12	52	Cisplatin 40mg BSA weekly i.v.

*potentially additional biomarkers, dependent on validation cohort and modeling inverse Pocock design (n=3)

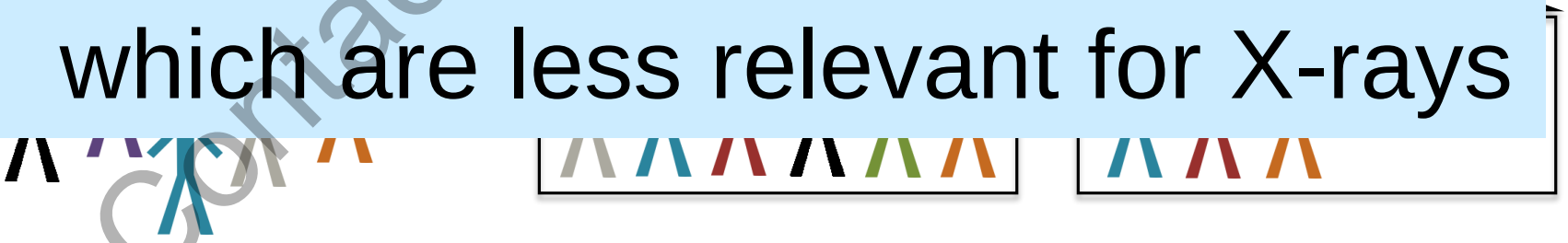
Personalized precision oncology





Personalized precision oncology

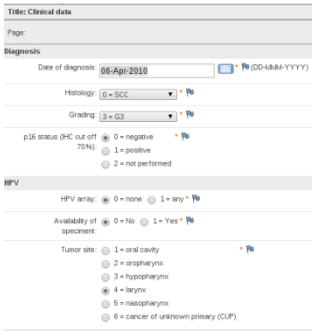
- Small numbers per center
- Particle trials more affected than photon trials:
  - less centers
  - less patients,
  - additional stratification factors which are less relevant for X-rays



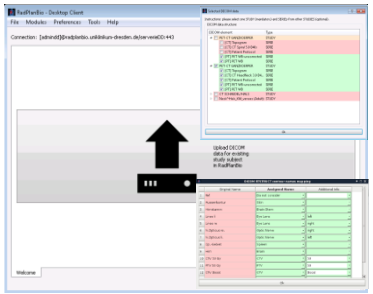
DOSE PLAN DATA BANKS
RADPLANBIO (DKTK ROG)

1. Clinical data

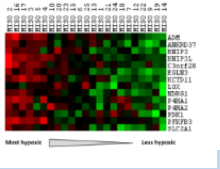
eCRF



DICOM Data

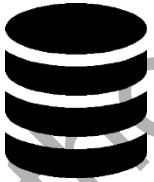


Bio-Data



2. Dataexport

- Data sets
- Statistics
-DICOM data port (offline)
-DICOM data port (online = WADO)
- ….



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journal homepage: www.thegreenjournal.com

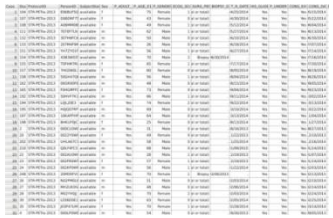
…eating a data exchange strategy for radiotherapy research: Towards federated databases and anonymised public datasets

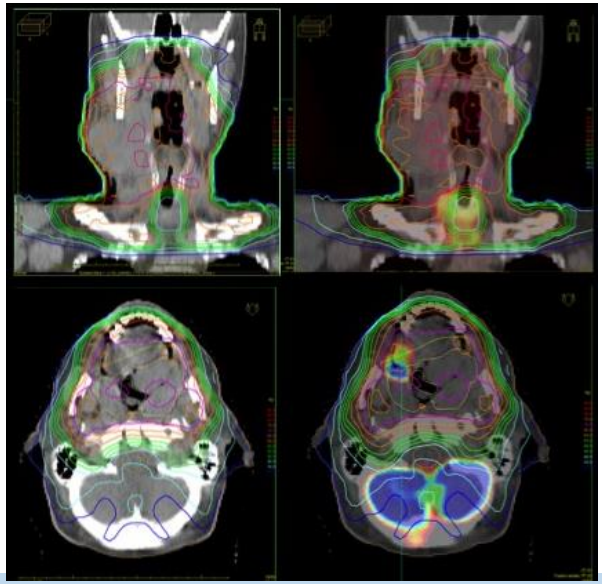
Tomas Skripcak [a,*], Claus Belka [b], Walter Bosch [c], Carsten Brink [d,ae], Thomas Brunner [e], Volker Budach [f], Daniel Büttner [a], Jürgen Debus [g], Andre Dekker [h], Cai Grau [i], Sarah Gulliford [j], Coen Hurkmans [k,l,m], Uwe Just [n], Mechthild Krause [a,n,o,p], Philippe Lambin [h], Johannes A. Langendijk [q], Rolf Lewensohn [r], Armin Lühr [a,s], Philippe Maingon [t,r], Michele Masucci [s], Maximilian Niyazi [b], Philip Poortmans [t], Monique Simon [e], Heinz Schmidberger [u], Emiliano Spezi [v], Martin Stuschke [w], Vincenzo Valentini [x], Marcel Verheij [y], Gillian Whitfield [z], Björn Zackrisson [aa], Daniel Zips [ab,ac,ad], Michael Baumann [a,n,o,p]

[a] German Cancer Consortium (DKTK) Dresden and German Cancer Research Center (DKFZ) Heidelberg; [b] German Cancer Consortium (DKTK) Munich and German Cancer Research Center (DKFZ) Heidelberg, Germany; [c] Dept. of Radiation Oncology, Washington University, St. Louis, MO, USA; [d] Laboratory of Radiation Physics, Odense University Hospital, Odense, Denmark; [e] German Cancer Consortium (DKTK) Freiburg and German Cancer Research Center (DKFZ) Heidelberg; [f] German Cancer Consortium (DKTK) Berlin, German Cancer Research Center (DKFZ) Heidelberg; [g] German Cancer Consortium (DKTK) Heidelberg and German Cancer Research Center (DKFZ) Heidelberg, Germany; [h] Dept. of Radiation Oncology (MAASTRO), GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands; [i] CIRRO Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; [j] Joint Department of Physics, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, London, UK; [k] Dept. of Radiation Oncology, Catharina Hospital, Eindhoven, The Netherlands; [l] EORTC-Radiation Oncology Group; [m] EORTC-Global Clinical Trial QART Harmonisation Group, Brussels, Belgium; [n] Dept. of Radiation Oncology, Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden; [o] OncoRay – National Center for Radiation Research in Oncology, Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden and Helmholtz-Zentrum Dresden-Rossendorf; [p] Institute of

3. Data analysis

- Advanced (Re) TPS
- Spatially resoluted – dose corrected outcome
- Radiomics
- TCP/NTCP
- Complex models
- trial hypotheses
- secondary analysis
- machine learning
- …





But this is not all…

Motion, anatomic changes during treatment, biological changes during treatment

Taking full advantage of particle therapy in terms of physics requires:

- Full image guidance (real time)
- Reduced range uncertainties (real time beam imaging)
- In vivo dosimetry
- Highest level treatment planning
- Adaptive algorithms incluing all items above
- Very rapid and exact dose delivery (repaiting, tracking)
- ....

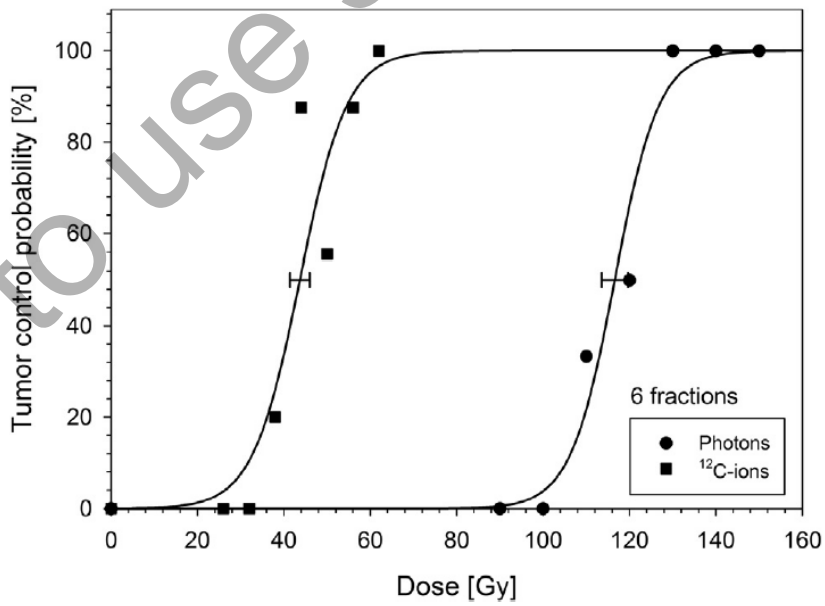
True clinical precision particles vs. photons

Parameter	Photons	Particles
High dose conformity to target volume	precise	In some pts. more precise
Irradiated volume	large	smaller
Image guidance during treatment	3D (or 4D) IG clinically well established	in its infancy
Beam position control	clinically well established	sporadic (research setting)
In vivo dosimetry	available but clinically not well established	not available
Full feed back loop	yes	no
Clinical (high level) evidence for relevant normal tissue sparing	yes for many sites	very little

But this is not all…

Lung, Mice, 200 MV P+

Time after irradiation	Number of fractions	DL50/Gy		RBE*
		^{60}Co	Protons	
180 days	1	12.0 (10.8–13.1)	11.5 (10.3–12.7)	1.04
	3	17.9 (15.2–20.0)	16.4 (13.8–18.5)	1.09
	10	27.7 (19.8–31.1)	32.2 (28.0–46.3)	0.86
210 days	1	10.9 (9.3–12.2)	9.1 (7.3–10.4)	1.20
	3	16.3 (13.2–18.4)	15.2 (12.4–17.3)	1.07
	10	26.1 (21.0–19.1)	27.2 (24.2–31.0)	0.96
240 days	1	9.6 (7.7–11.1)	7.3 (4.8–8.9)	1.33
	3	14.2 (9.2–16.7)	13.8 (9.7–16.2)	1.02
	10	23.7 (11.7–27.7)	22.5 (14.2–26.3)	1.05
270 days	1	8.6 (6.4–10.1)	5.5 (2.5–7.4)	1.55
	3	12.4 (3.7–15.7)	11.7 (3.8–14.8)	1.06
	10	21.1 (7.8–25.4)	20.6 (11.4–24.1)	1.02



Study	RBE ± SE (90% CI)
1 Fraction*	2.30 ± 0.08 (2.17-2.44)
2 Fractions*	2.39 ± 0.16 (2.15-2.68)
6 Fractions	2.67 ± 0.15 (2.43-2.94)

But this is not all…

Biology based treatment stratification and treatment planning requires:

- RBE assessment for a large range of beam qualities, energies and positions on the depth curve and beyond
- RBE assessment for a large range of clinical relevant cell systems and organ systems
- In the context of combinations used in patients
- Under knowledge of emerging molecular biomarkers and functional imaging
- Mechanistic understanding
- Systems biology approaches for development of comprehensive models for patient use

Dose (Gy)

But this is not all…

Currently particle therapy is by far more expensive and by far more dependent on a huge team of highly skilled experts

Range of beam is needed

Novel approaches need to be investigated (discovery and basic research) and translated into the clinics (development)

Education and Training

Societal challenges: Innovation and health economy research

European particle network

Brussels Meeting 2015:
All European centers, ESTRO, EORTC, CERN, ENLIGHT/ULICE

- Scoring and endpoints
- Technology, dosimetry, QA
- Trial inventory (Website); towards joint clinical trials
- Image guidance in PT
- TPS in PT
- Radiobiology, RBE
- Health Economy

1st Particle Therapy Meeting, Brussels (8th April 2015)

WP	Title	Suggested Coordinators
1	**Scoring of normal tissue reactions and tumor response particle/photon RT; endpoint definitions, outcome database**	Hans Langendijk, Mechthild Krause, Roberto Orrechia
2	**Dose assessment, quality assurance, dummy runs, technology inventory**	Dietmar Georg, Oliver Jäckel, Sairos Safai
3	**Trials inventory (website); „Towards joint clinical trials“**	Karin Hausterman, Cai Grau, Daniel Zips, Jacques Balosso
4	**Image Guidance in particle therapy**	Aswin Hoffmann, Alessandra Bolsi
5	**TPS in particle therapy**	Hakan Nystrom, Tony Lomax
6	**Radiobiology, RBE**	Bleddyn Jones, Jörg Pawelke, Jan Alsner, Martin Prutschy, Manjit Dosanjh
7	**Health Economy**	Yolande Lievens, Klaus Nagels

+ Education and Training

2nd Particle Therapy Meeting, Brussels, 2016

----------SAFE THE DATE----------

2nd Particle Therapy Meeting

When: Wednesday, May 18th 2016

Where: ESTRO office, Brussels, Belgium

Model based approach: In silico trial for trial design

Proton vs. photon comparison for H&N

Serie I: 10 # × 2 Gy PTV adjuvant

Patient stratification (Hypoxia PET)

Serie II: 15 # × 2 Gy PTV adjuvant

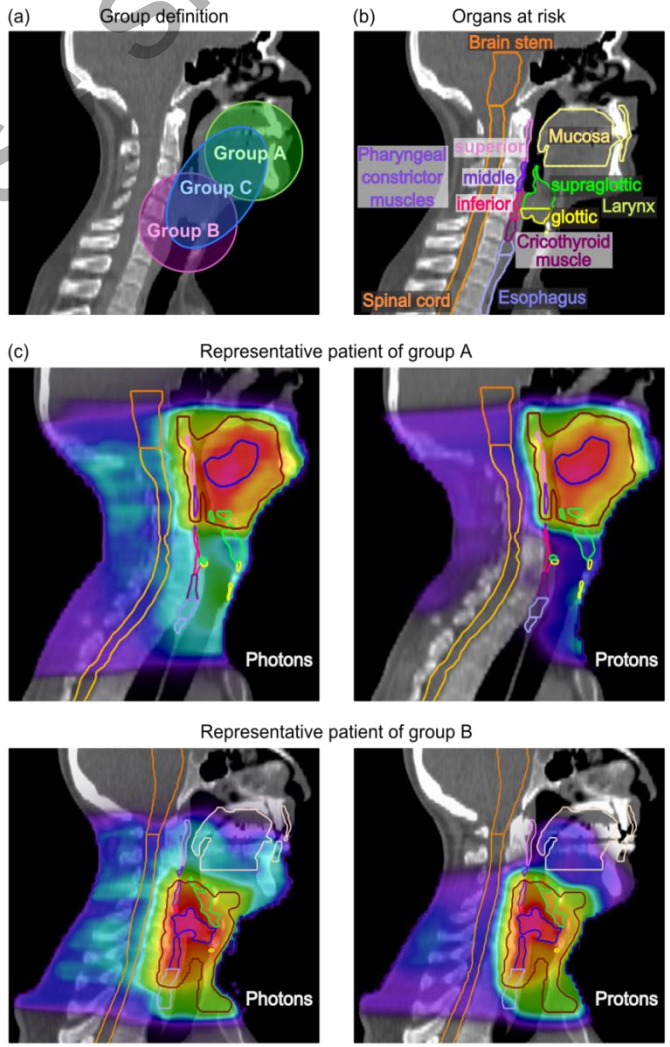
Serie II: 15 # × 2 Gy PTV adjuvant + SIB 2.3 Gy / 2.6 Gy

Adaption

Serie III: 11 # × 2 Gy Boost

Serie III: 11 # × 2 Gy Boost + SIB 2.3 Gy / 2.6 Gy

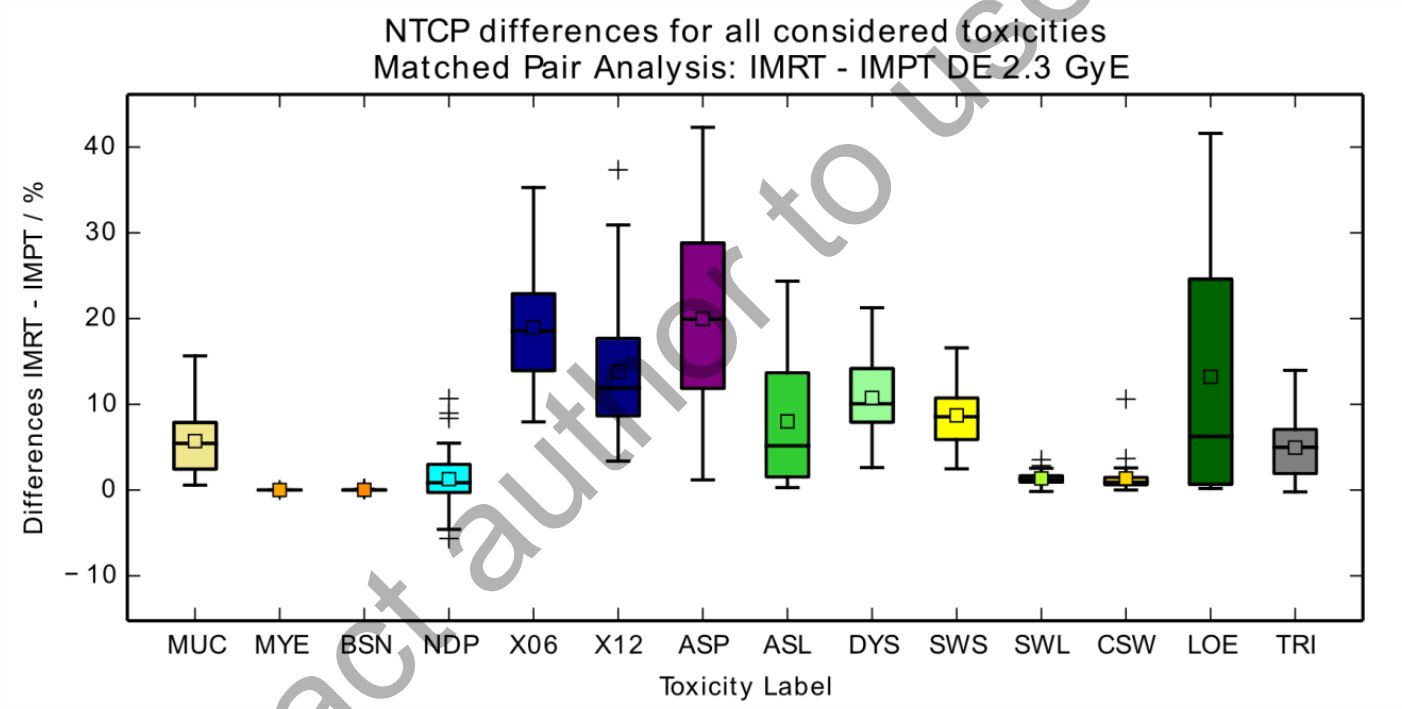
- Two dose escalation steps via simultaneous integrated boost (SIB)
- IMRT vs. PBS
- Non-rigid (dose) deformation + summation
- Subgroup analysis



Jakobi et al., IJROBP 2015

Model based approach: in silico trial for trial design

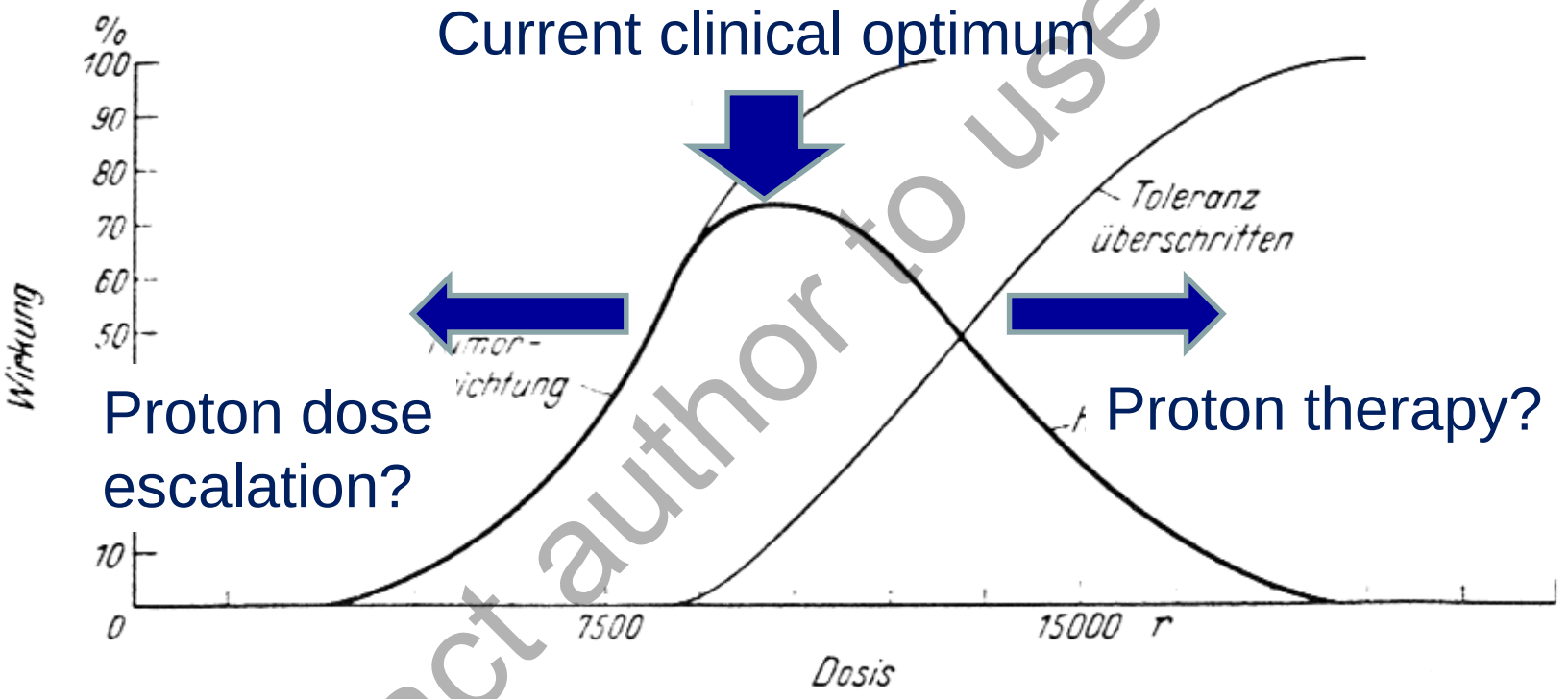
Proton vs. photon comparison for H&N



MUC: Oral mucositis
MYE: Myelopathy
BSN: Brain stem necrosis
NDP: Nerve damage of brachial plaxus
X06: Xerostomia after 6 months
X12: Xerostomia after 12 months
ASP: Aspiration based on pharyngeal constrictor muscles
ASL: Aspiration based on larynx
DYS: Physician-rated swallowing dysfunction
SWS: Patient-rated problems swallowing solid food
SWL: Patient-rated problems swallowing liquids
CSW: Patient-rated choking when swallowing
LOE: Laryngeal oedema
TRI: Trismus

Jakobi et al., IJROBP 2015

Particle therapy: clinical research



*) Vortrag vor der Deutschen Röntgengesellschaft am 24. April 1936

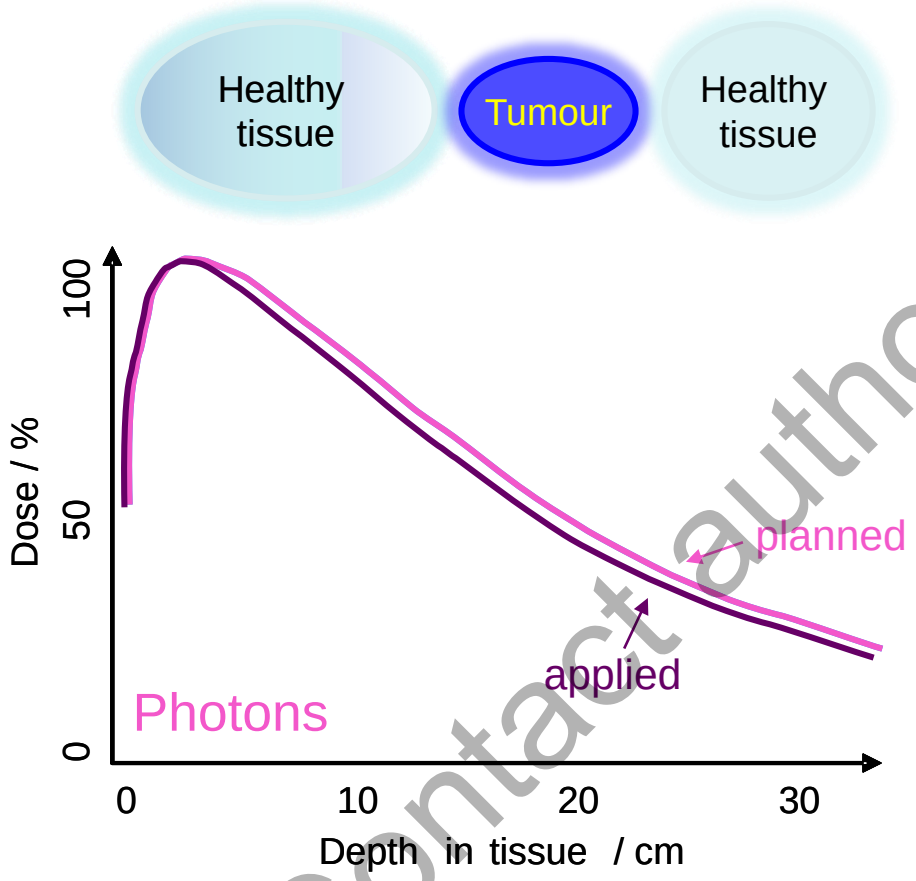
Holthusen, Strahlentherapie 57: 254-268,1936

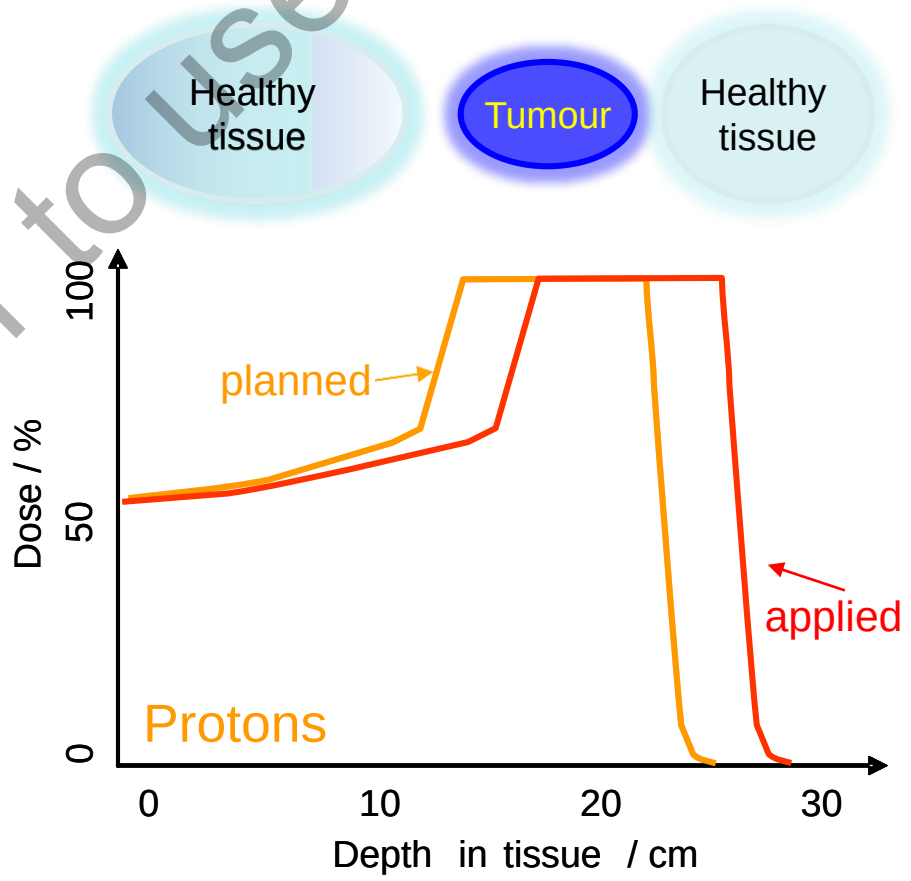
„There‘s no such thing as a free lunch“

El Paso Herald Post, 1936
Milton Friedman, 1975

Overall treatment system, e.g. IGRT

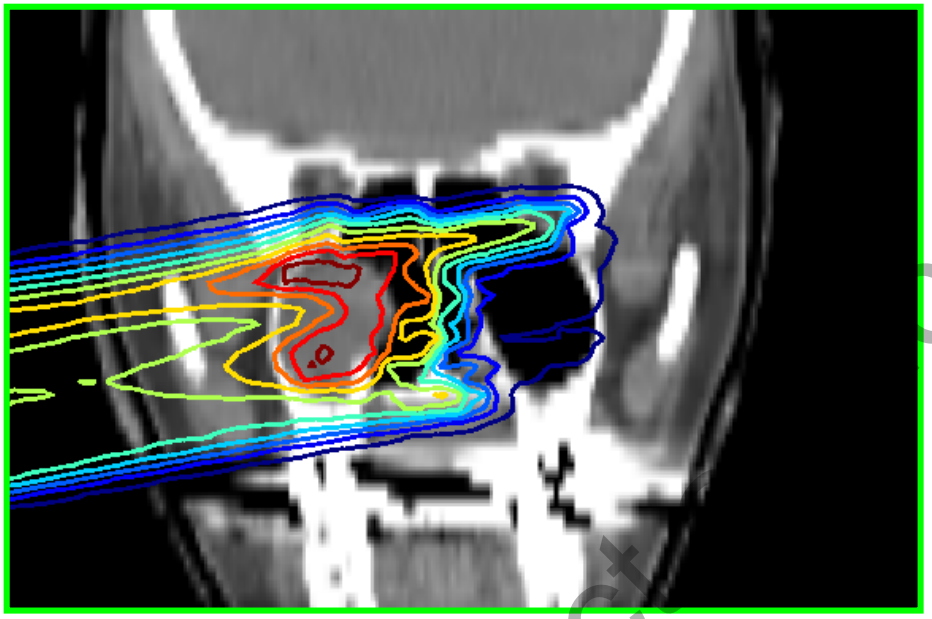
Range uncertainties



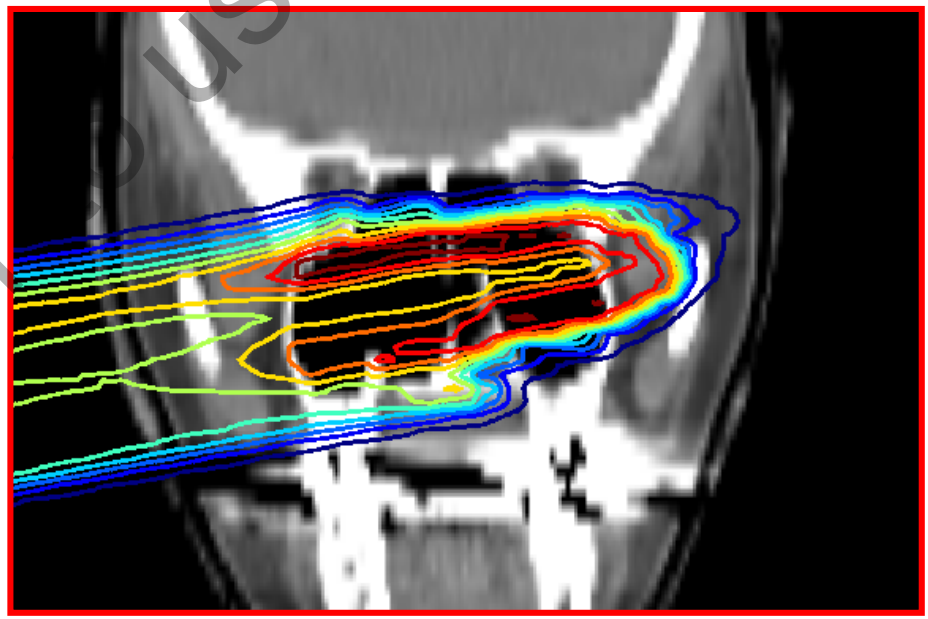


High precison particle therapy: Range uncertainties

Planned

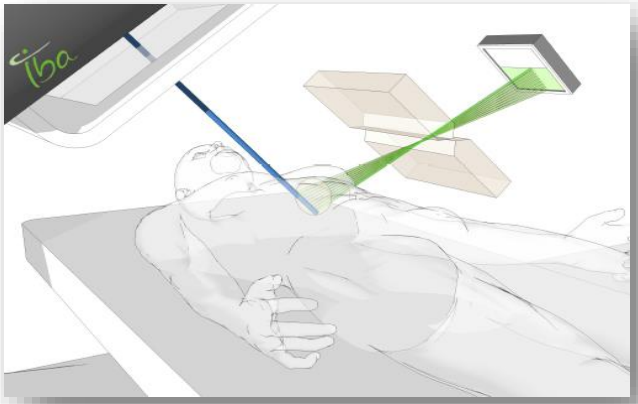


Irradiated

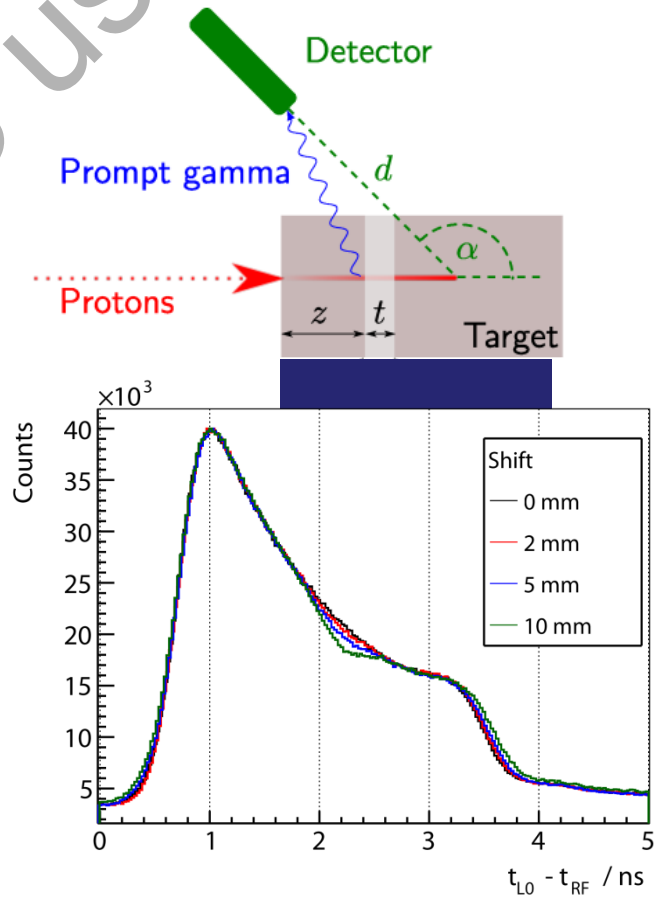


Reducing uncertainties: In vivo range verification

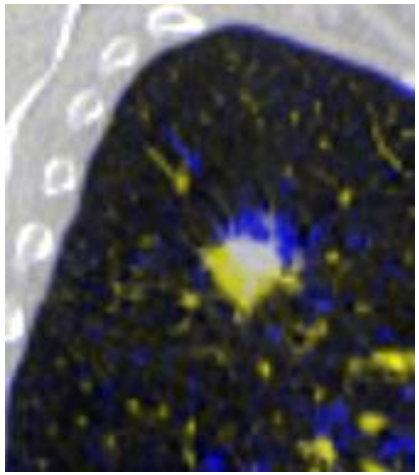
Prompt γ-ray imaging

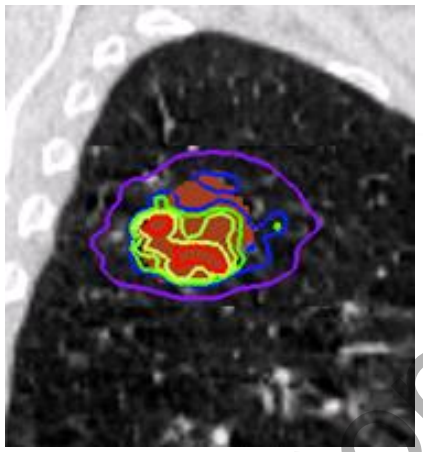


Prompt γ-ray timing (PGT)



Motion control robust TP for active spot scanning (particles)

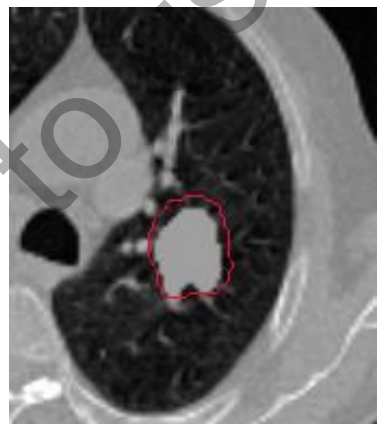


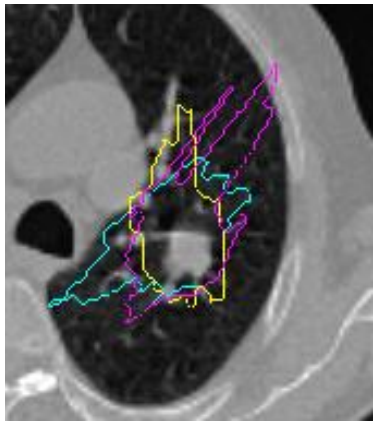


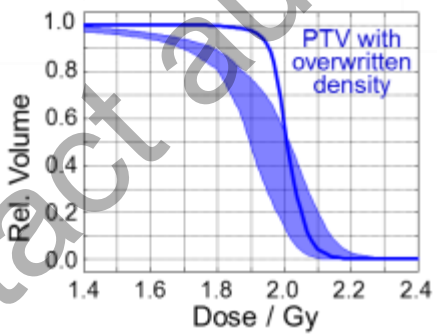
PTV with overwritten density

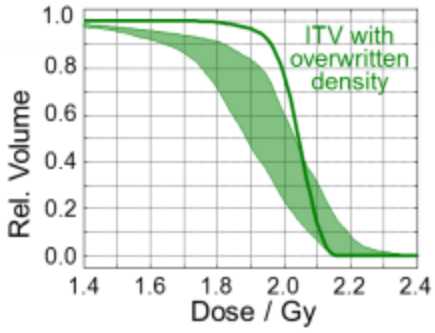
ITV with overwritten density

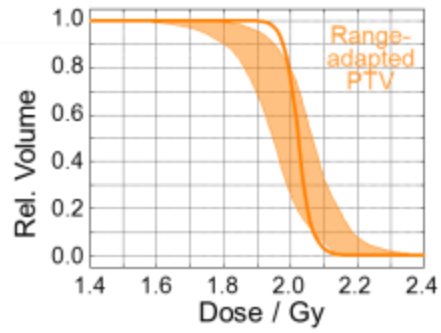
Range adapted ITV





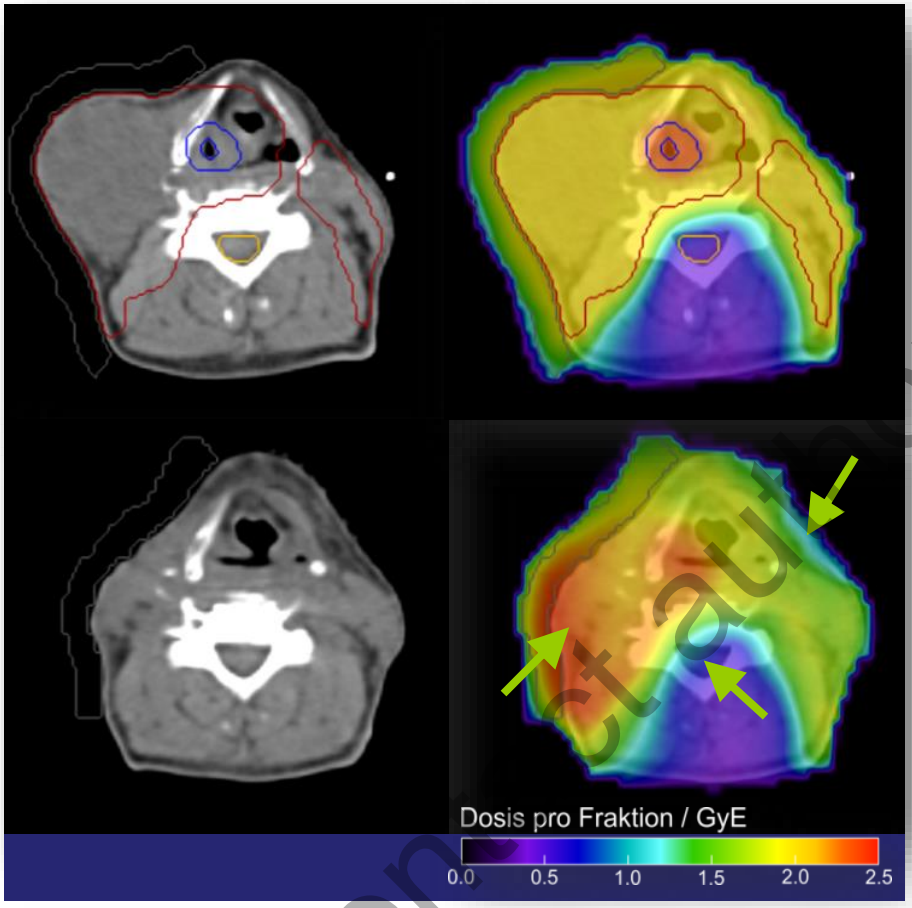


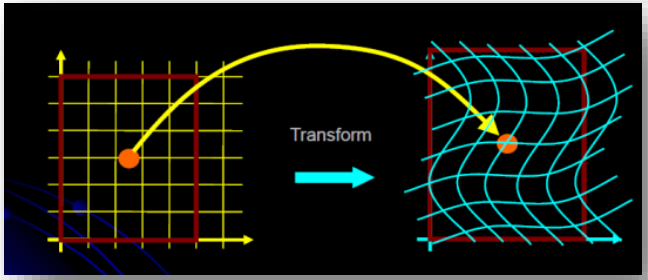


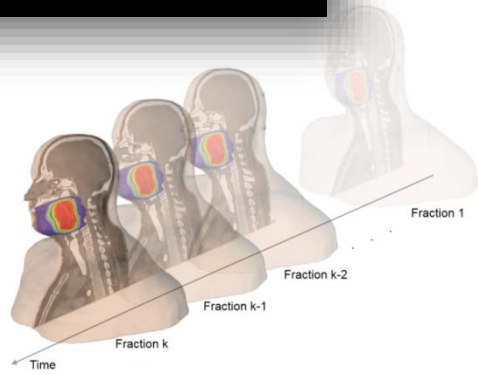


A. Jakobi, Chr. Richter
in cooperation with PSI

High precison particle therapy
Image guidance and adaptive planning

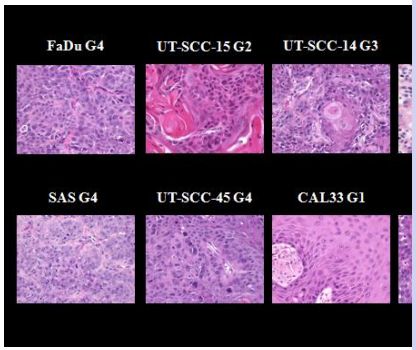


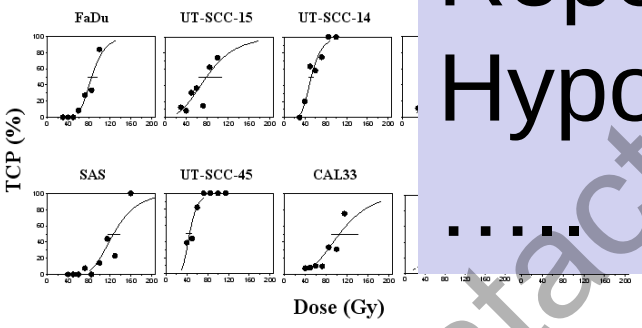




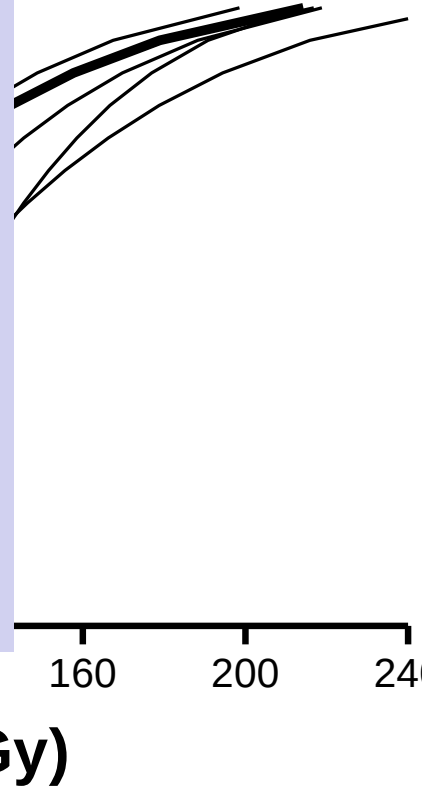
Impact of biological heterogeneity on particle therapy research

10 human SCC in nude mice, @ 6 mm, 30 f/ 6w



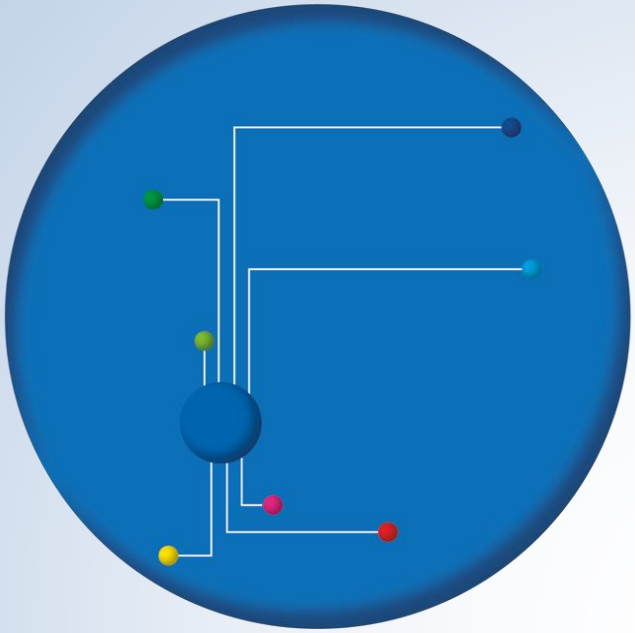


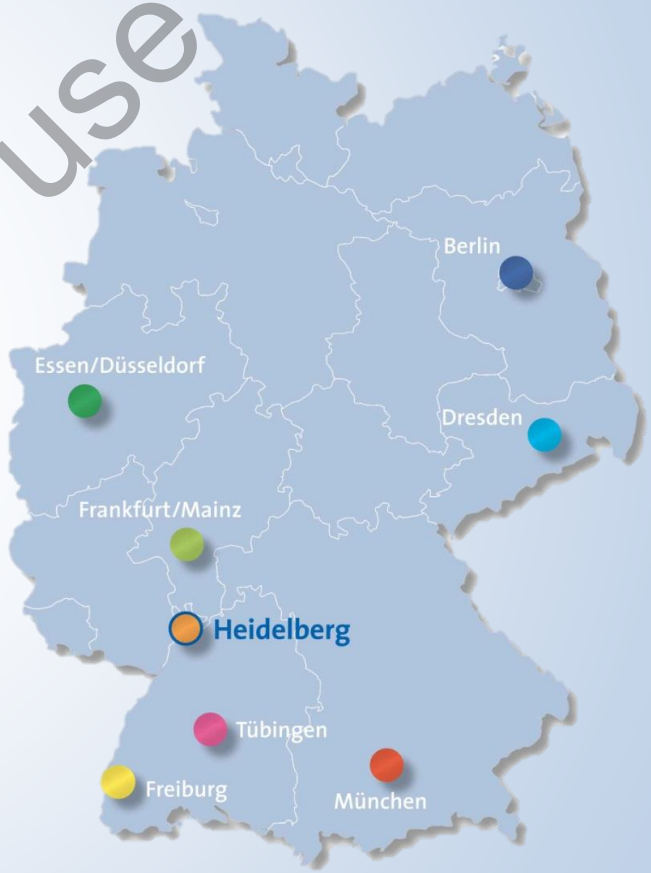
Number/density of CSC
Cellular radiosensitivity
Repair
Repopulation
Hypoxia/Reoxygenation
.....



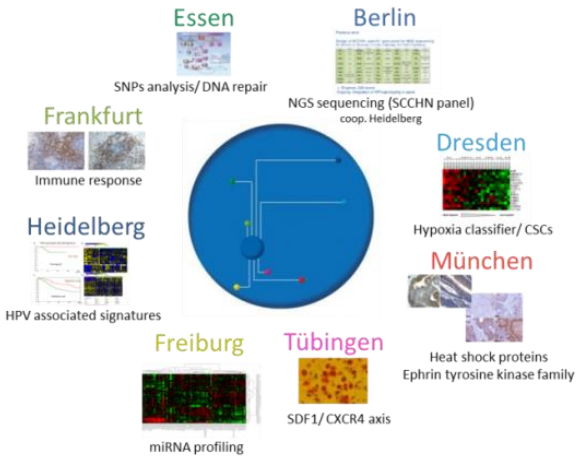
Yaromina et al., *Radiother. Oncol* 83: 304-310, 2007 and unpublished

Germany Cancer Consortium (DKTK) Radiation Oncology Group (ROG)





MOLECULAR STRATIFICATION FOR RADONC: MULTICENTER RETROSPECTIVE/PROSPECTIVE TRIAL (RCT, HNSCC, POSTOP, DEFINITE)



Retrospective exploration [2012-2015]

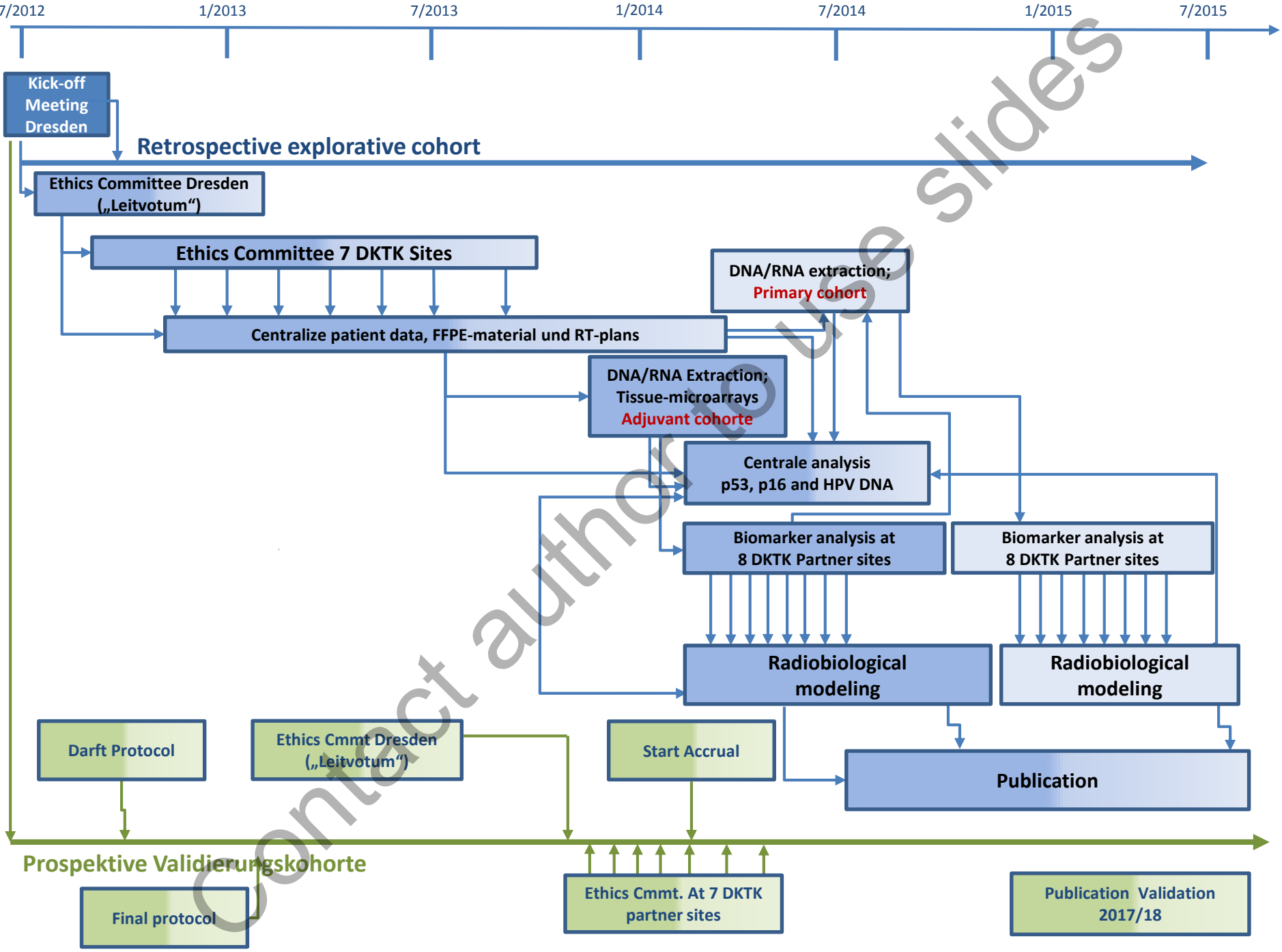
- RT 2004 to 2012 (Backwards inclusion)
- Candidate-biomarker analysis since 2013
- Radiobiological modelling since 2014
- Final hypotheses for validation 2016

Validation of hypotheses

Prospective validation trial [2014-2018]

- Recruitment 2014-2016
- Biomarker-Evaluation 2016/ 2017
- Sampling of outcome data 2014 bis 2018
- Final Analysis of trial 2018

Interventional trial [2016/17-...]



MOLECULAR STRATIFICATION FOR RADONC: MULTICENTER RETROSPECTIVE/PROSPECTIVE TRIAL (RCT, HNSCC, POSTOP, DEFINITE)

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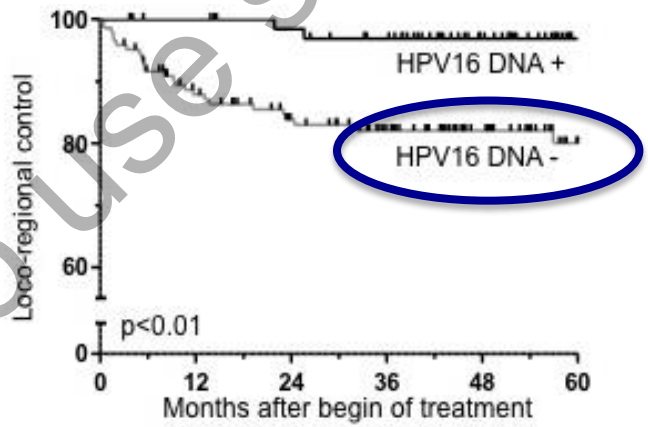
HPV in postoperative RT of oropharynx

HPV16 DNA status is a strong prognosticator of loco-regional control after postoperative radiochemotherapy of locally advanced oropharyngeal carcinoma: Results from a multicentre explorative study of the German Cancer Consortium Radiation Oncology Group (DKTK-ROG)

Fabian Lohaus [a,i,j,1], Annett Linge [a,i,j,1], Inge Tinhofer [b,k], Volker Budach [b,k], Eleni Gkika [c,l], Martin Stuschke [c,l], Panagiotis Balermpas [m], Claus Rödel [d,m], Melanie Avlar [e,n], Anca-Ligia Grosu [e,o], Amir Abdollahi [f,p,q,r], Jürgen Debus [f,p,q,s], Christine Bayer [g], Claus Belka [g,t], Steffi Pigorsch [g,u], Stephanie E. Combs [g,u], David Mönnich [h,v], Daniel Zips [h,v], Cläre von Neubeck [a,j], Gustavo B. Baretton [a,w,x], Steffen Löck [j], Howard D. Thames [z], Mechthild Krause [a,j,j,y], Michael Baumann [a,i,j,y,*], for the DKTK-ROG

post-op RCT

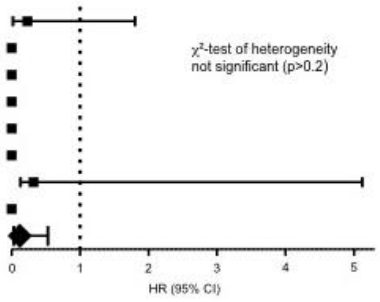


Patients at risk

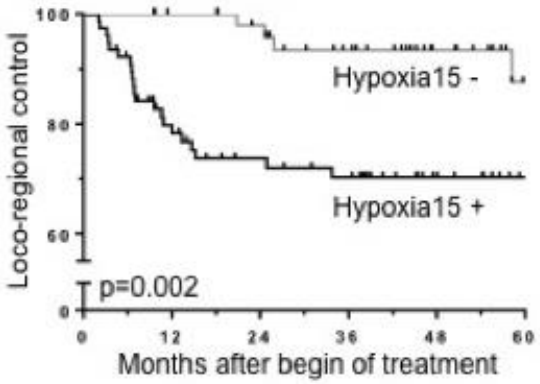
HPV16 DNA +	72	69	65	58	43	24
HPV16 DNA -	143	116	102	86	60	36

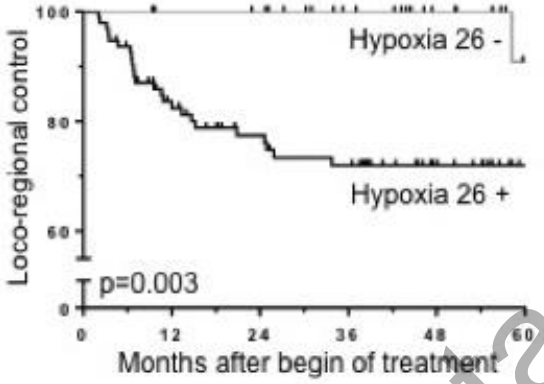
Treatment centre	Loco-regional control, HR (95% CI)		HPV16 DNA positive Events	HPV16 DNA positive Total	HPV16 DNA negative Events	HPV16 DNA negative Total
Centre 1	0.23	(0.02-1.80)	1	12	9	30
Centre 2	0	*	0	7	4	20
Centre 3	0	*	0	11	3	20
Centre 4	0	*	0	10	3	20
Centre 5	0	*	0	9	4	23
Centre 6	0	*	0	4	2	17
Centre 7	0.32	(0.02-5.12)	1	13	1	4
Centre 8	0	*	0	6	1	9
Overall	**0.13**	**(0.03-0.54)**	**2**	**72**	**27**	**143**

* No CI was calculated in case of no event in the HPV16 DNA positive group

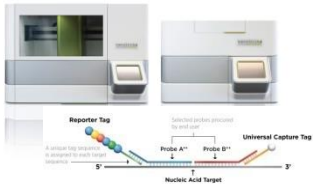


MOLECULAR STRATIFICATION FOR RADONC: MULTICENTER RETROSPECTIVE/PROSPECTIVE TRIAL (RCT, HNSCC, POSTOP, DEFINITE)





Nanostring Technology

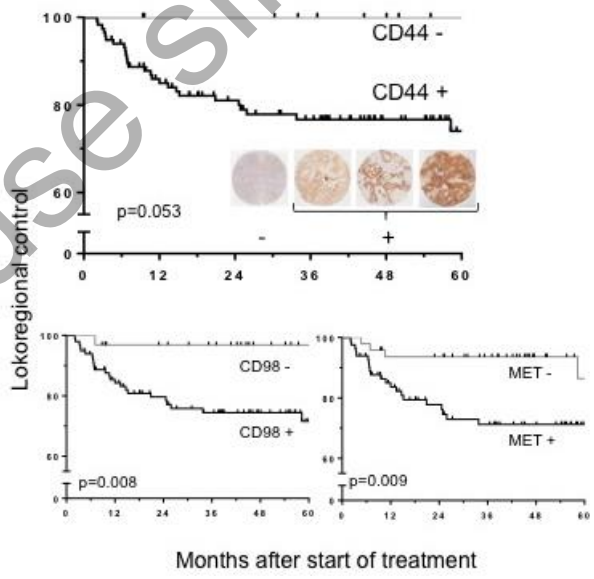


15 gene signature (Arhus)

26 gene signature (Manchester)

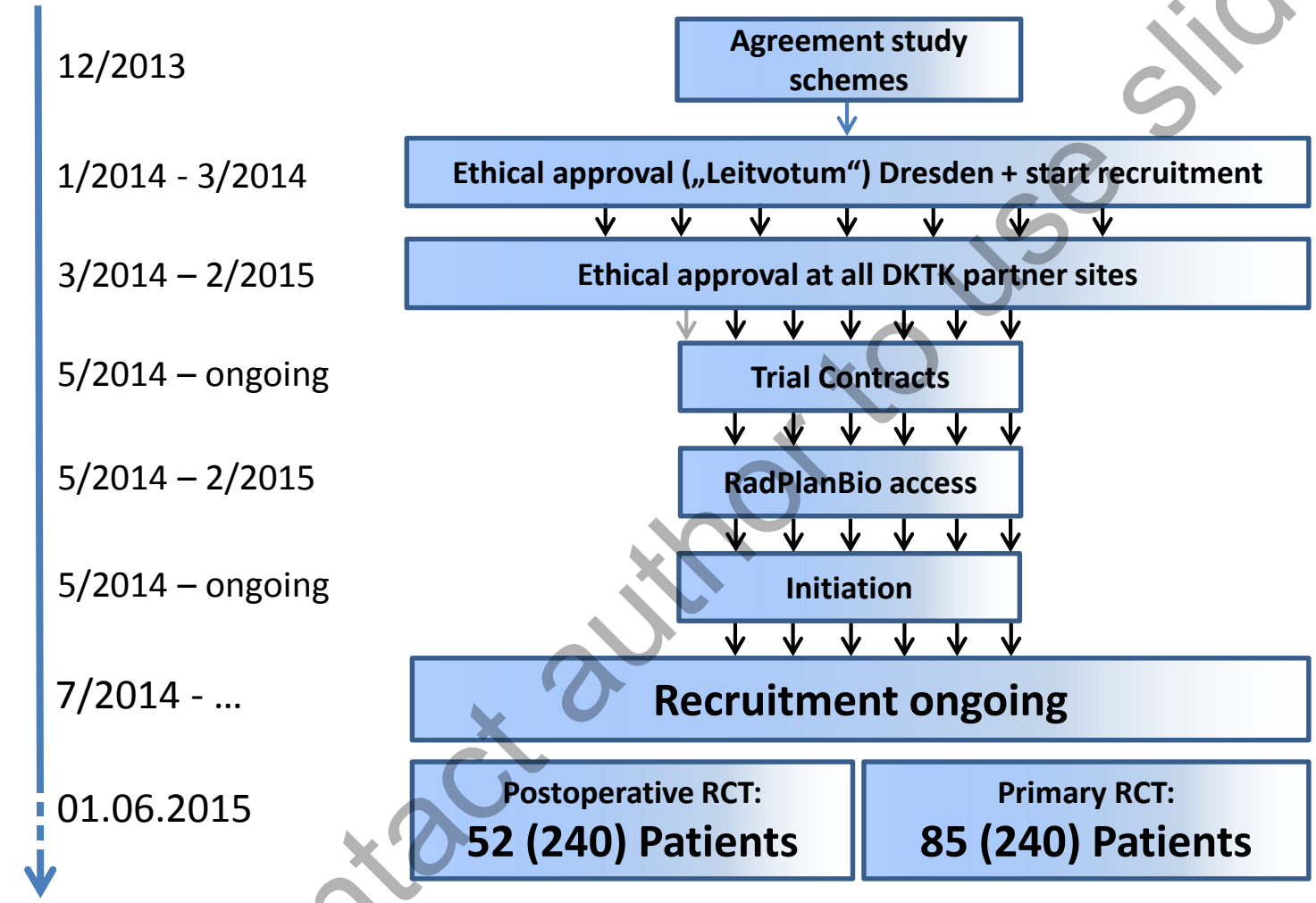
with local reccurrence

without local recurrence

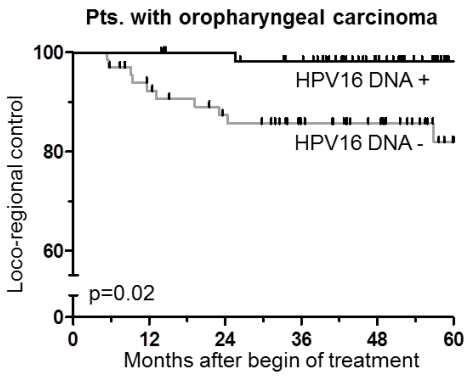


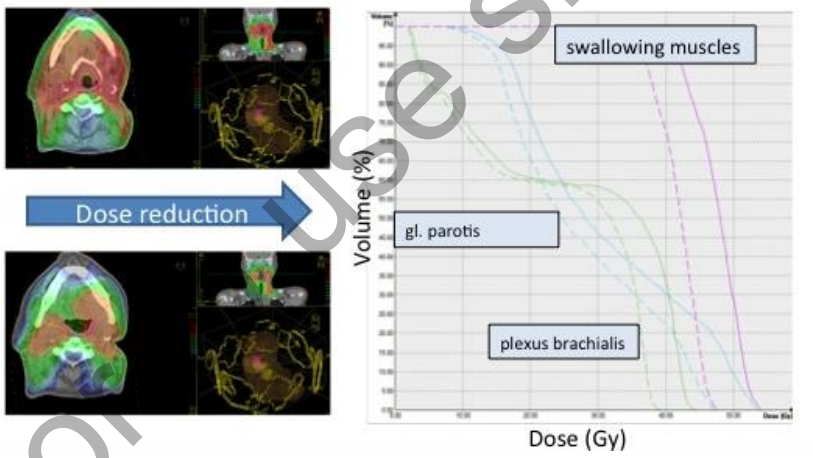
		15-gene signature Hypoxia		26-gene signature Hypoxia	
		Low	High	Low	High
CD44	0	21	16	23	14
	1	48	96	42	102
		R=0.194	p=0.009	R=0.277	p<0.001
MET	0	52	42	59	35
	1	27	75	13	89
		R=0.294	p<0.001	R=0.518	p<0.001
CD98	0	44	33	55	22
	1	23	84	17	102
		R=0.276	p<0.001	R=0.579	p<0.001

PROSPECTIVE TRIAL: RECRUITING



INTERVENTIONAL TRIAL: DOSE DE-ESCALATION POST-OP HNSCC





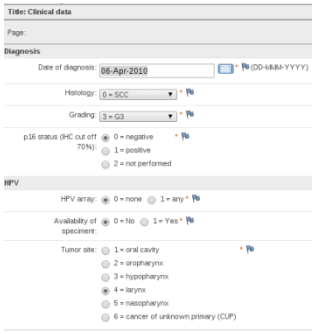
Dose level	Number of patients	RT-Dose (Gy)			Chemotherapy
		CTV A	CTV B	Σ	
1	30	44	16	60	Cisplatin 40mg BSA weekly i.v.
2*	30	40	12	52	Cisplatin 40mg BSA weekly i.v.

*potentially additional biomarkers, dependent on validation cohort and modeling inverse Pocock design (n=3)

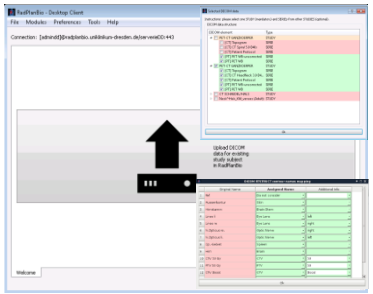
DOSE PLAN DATA BANKS
RADPLANBIO (DKTK ROG)

1. Clinical data

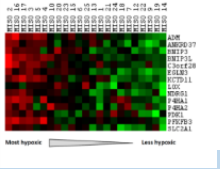
eCRF



DICOM Data

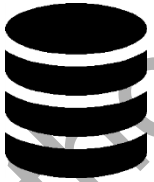


Bio-Data



2. Dataexport

- Data sets
- Statistics
-DICOM data port (offline)
-DICOM data port (online = WADO)
- ….



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…eating a data exchange strategy for radiotherapy research: Towards federated databases and anonymised public datasets

Tomas Skripcak [a,*], Claus Belka [b], Walter Bosch [c], Carsten Brink [d,ae], Thomas Brunner [e], Volker Budach [f], Daniel Büttner [a], Jürgen Debus [g], Andre Dekker [h], Cai Grau [i], Sarah Gulliford [j], Coen Hurkmans [k,l,m], Uwe Just [n], Mechthild Krause [a,n,o,p], Philippe Lambin [h], Johannes A. Langendijk [q], Rolf Lewensohn [r], Armin Lühr [a,s], Philippe Maingon [t,r], Michele Masucci [s], Maximilian Niyazi [b], Philip Poortmans [t], Monique Simon [e], Heinz Schmidberger [u], Emiliano Spezi [v], Martin Stuschke [w], Vincenzo Valentini [x], Marcel Verheij [y], Gillian Whitfield [z], Björn Zackrisson [aa], Daniel Zips [ab,ac,ad], Michael Baumann [a,n,o,p]

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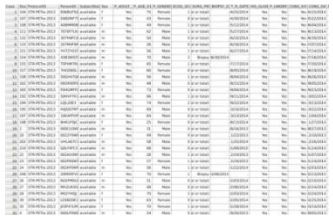
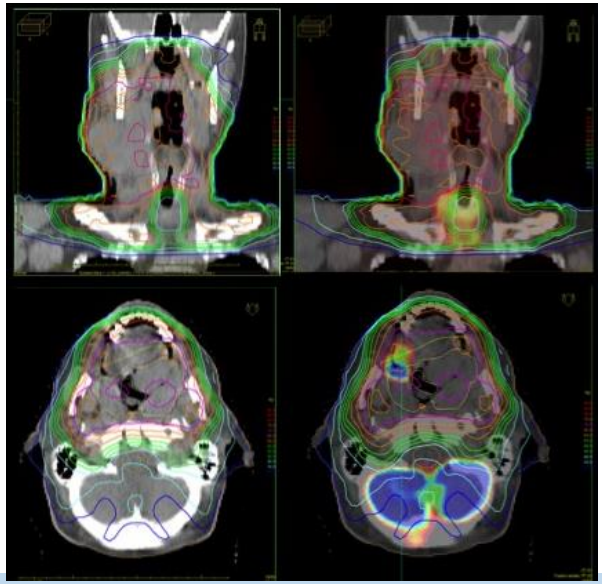
3. Data analysis

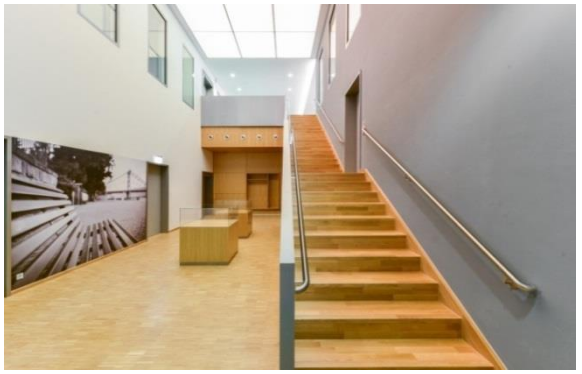
- Advanced (Re) TPS
- Spatially resoluted – dose corrected outcome
- Radiomics
- TCP/NTCP
- Complex models
- trial hypotheses
- secondary analysis
- machine learning
- …





Take home messages

- P+ have significant potential
- Mainly based on sparing of low and intermediate dose (little is known)
- TP, IGRT, Monitoring lags behind advanced photon therapy
- Model-based approaches and novel clinical designs needed
- Stratification: small numbers will hurt
- Networks and large treatment plan data banks needed



Universitäts Protonen Therapie Dresden

Klinik für Strahlentherapie OncoRay

Thanks!

State of the art

- R