HITRI plus
Heavy Ion Therapy Research Integration

Hypoxia

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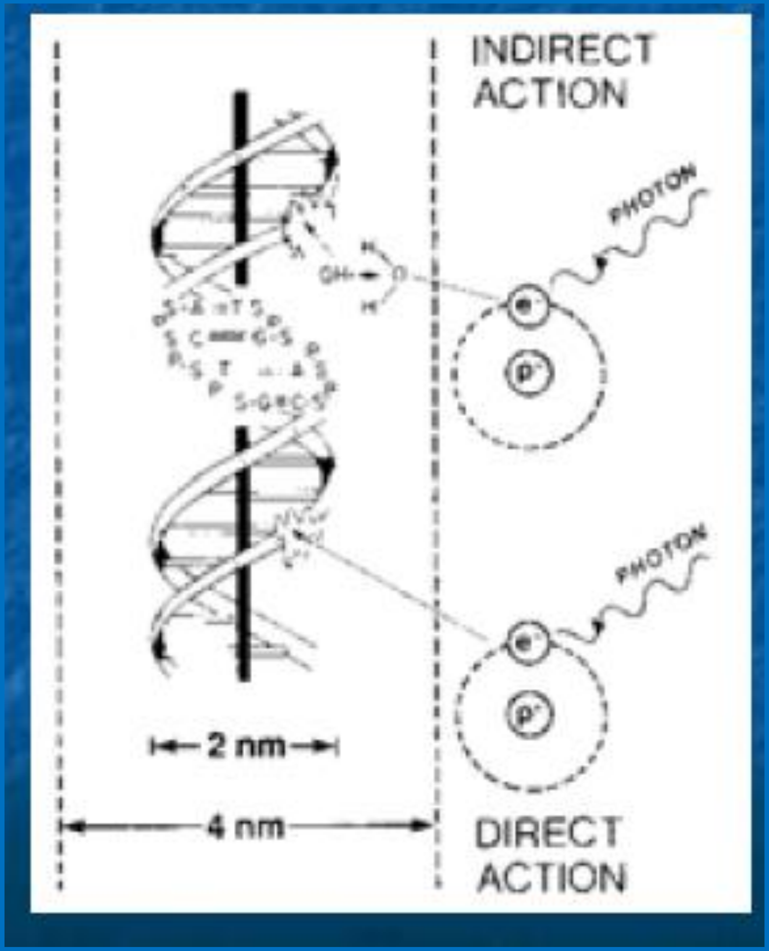
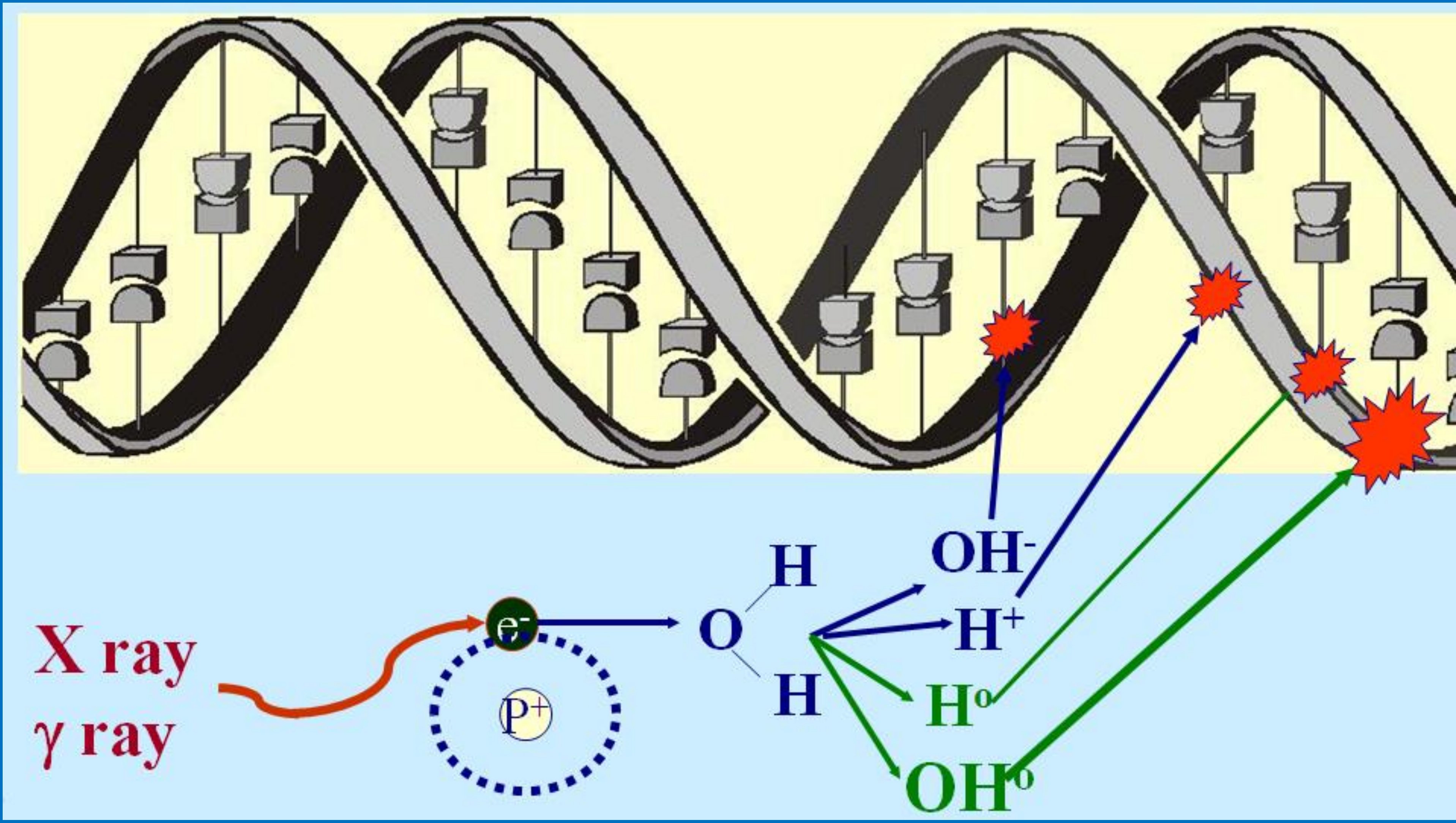
Direct vs. indirect effect of radiation



Indirect action



$$H^0 + OH^0 \rightarrow HOH$$

$$H^0 + H^0 \rightarrow H_2$$

$$OH^0 + OH^0 \rightarrow H_2O_2$$

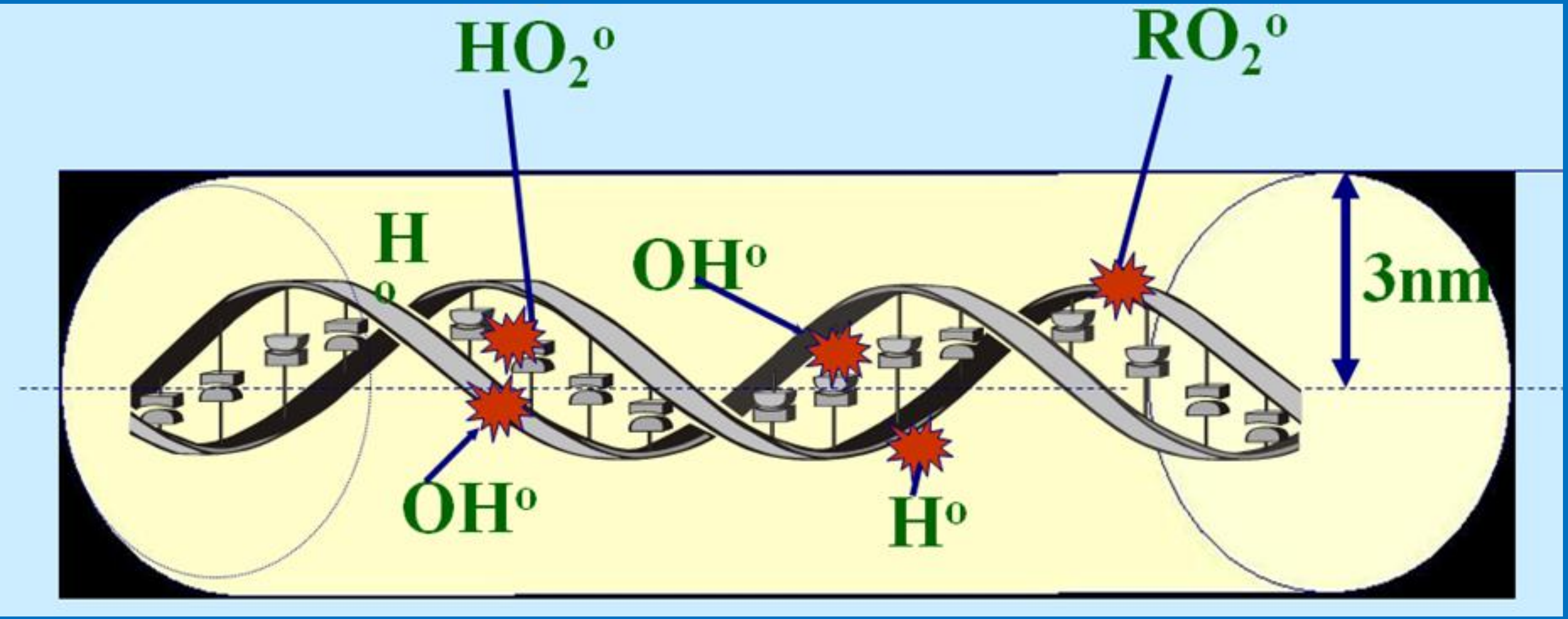
$$OH^0 + RH \rightarrow R^0 + HOH$$

Oxygen stabilizes free radicals

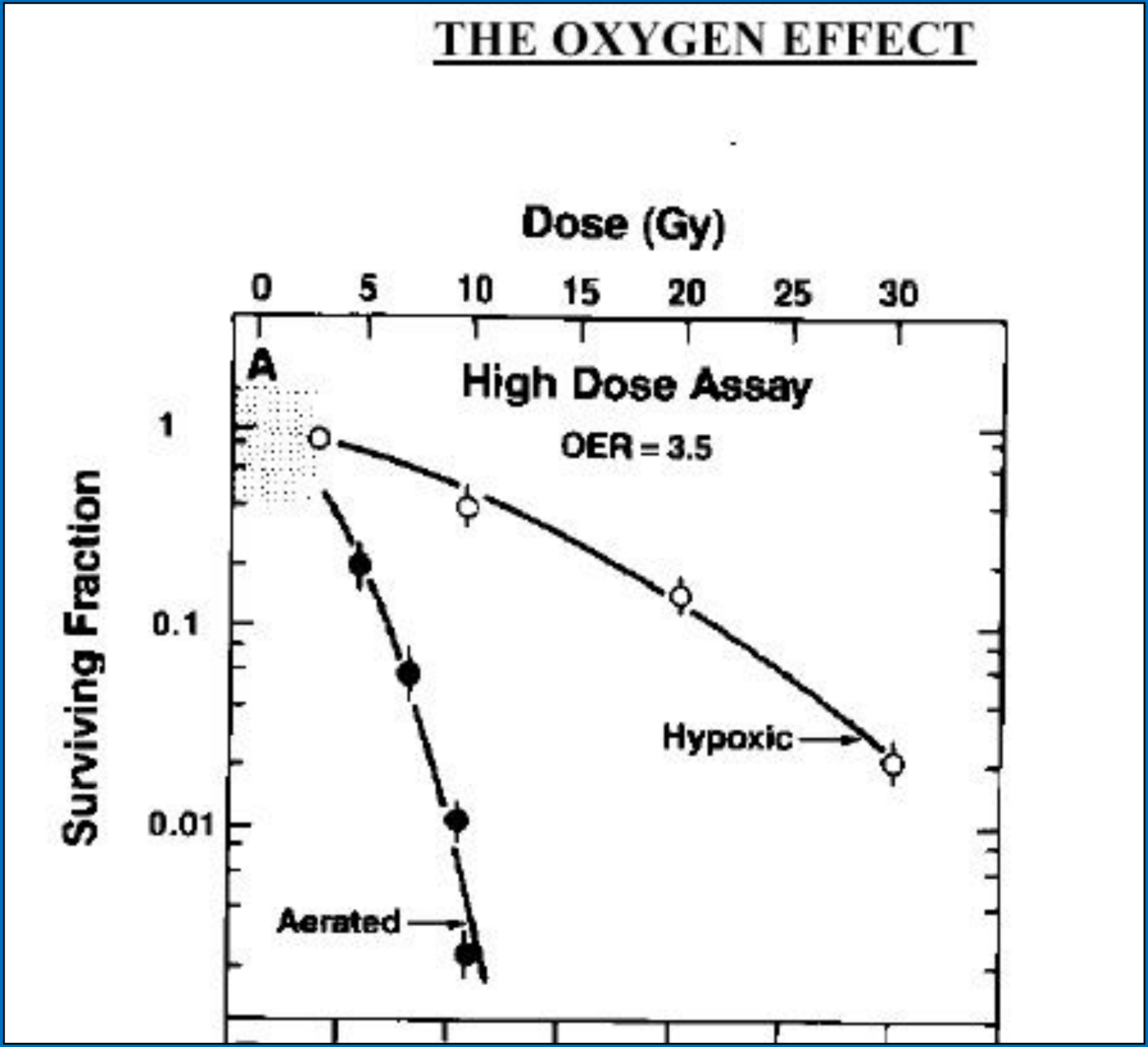
$$H^0 + O_2 \rightarrow HO_2^0$$

$$R^0 + O_2 \rightarrow RO_2^0$$

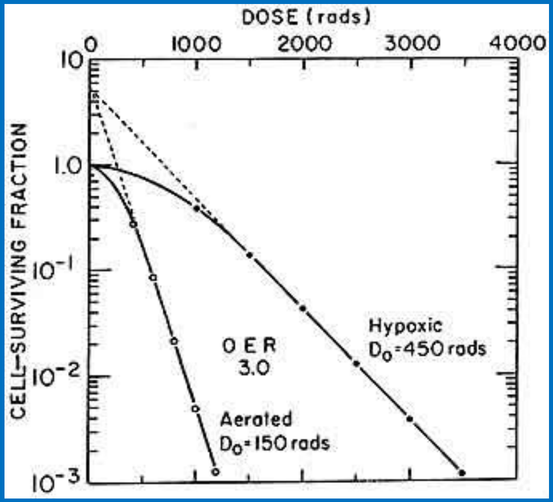
… so they can travel farther

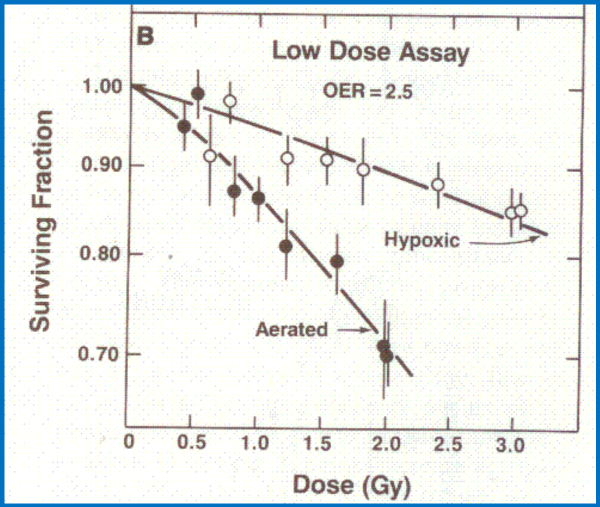


More oxygen → more cell killing with the same dose



OER (Oxygen Enhancement Ratio)

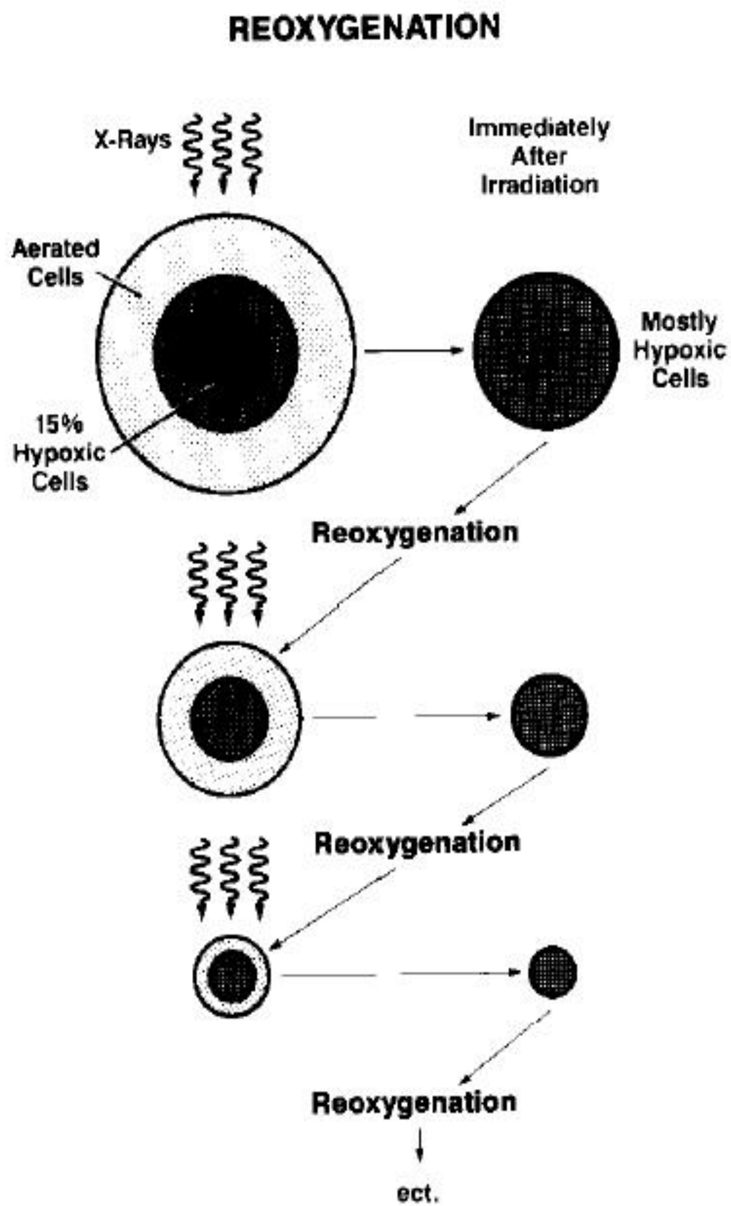




$$\textbf{OER} = \frac{\text{Dose required to cause effect without oxygen}}{\text{Dose required to cause effect with oxygen}}$$

A very big effect tipically:

OER = 2.5-3



Illustrating the process of reoxygenation. Tumors contain a mixture of aerated and hypoxic cells. A dose of x rays kills a greater proportion of aerated than hypoxic cells because they are more radiosensitive. Immediately after irradiation, most cells in the tumor are hypoxic. But the pre-irradiation pattern, tends to return due to the process of REOXYGENATION. If the radiation is given in a series of fractions separated in time sufficient for reoxygenation to take place, the presence of hypoxic cells does not greatly influence the response of the tumor.

Two **false** statements:

1. High LET radiation is insensitive to hypoxia

2. Carbon ion RT is high LET radiation

IOP Publishing Physics in Medicine and Biology
Phys. Med. Biol. 56 (2011) 3251–3268 doi:10.1088/0031-9155/56/11/006

Modelling of the oxygen enhancement ratio for ion beam radiation therapy

Tatiana Wenzl and Jan J Wilkens

Department of Radiation Oncology, Technische Universität München, Klinikum rechts der Isar, Ismaninger Str. 22, 81675 Munich, Germany

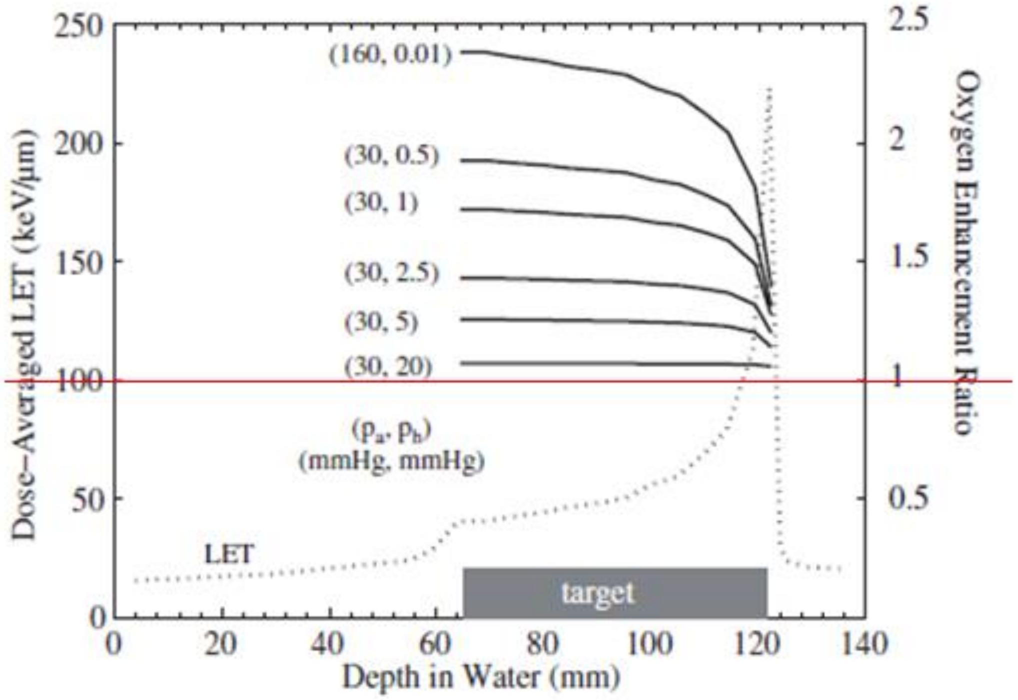
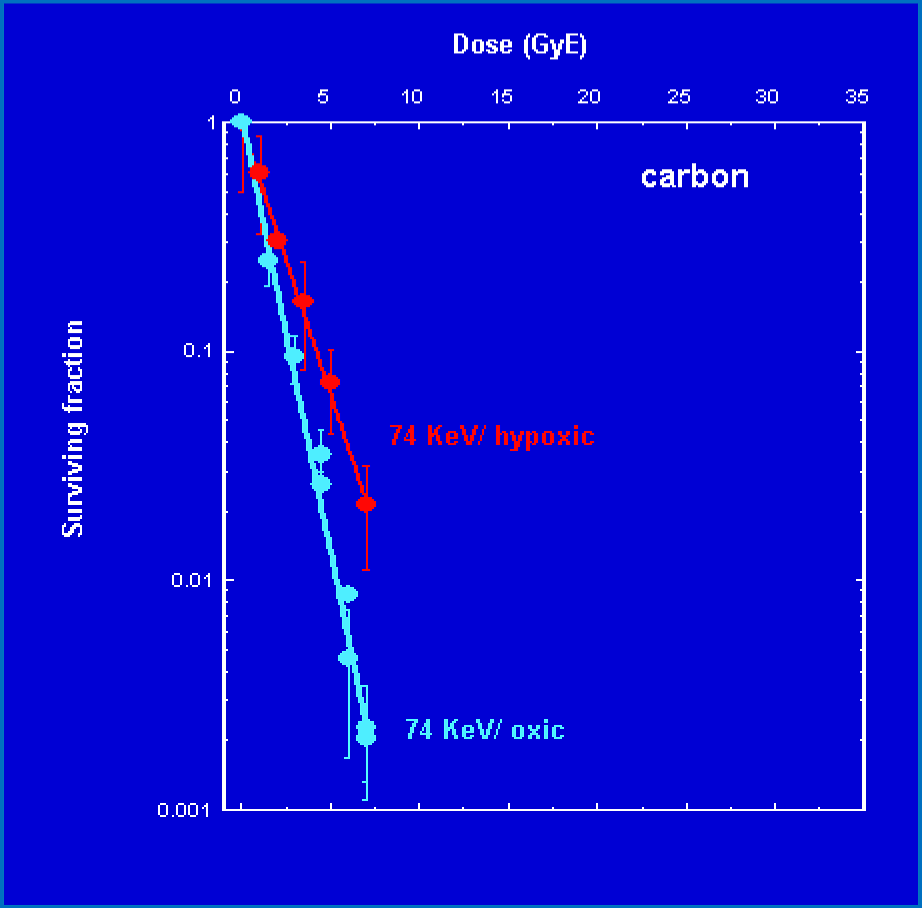
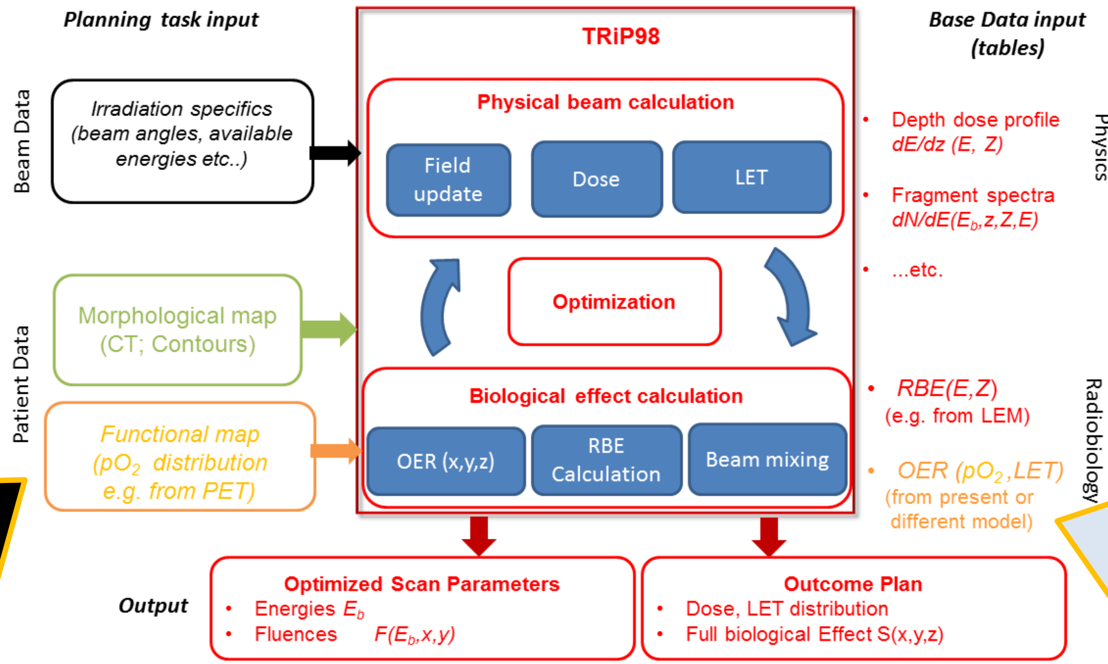


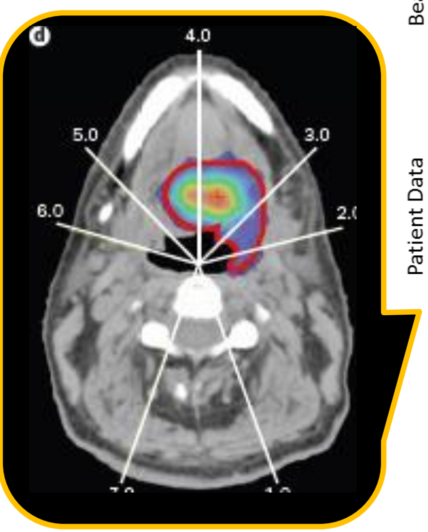
Figure 5. Calculated OER (right ordinate) as a function of LET and hence depth for a clinical carbon ion beam for various oxygen partial pressures. The data for LET as a function of depth (dotted line) were taken from Kohno *et al* (2005).

OER is not 1 for 74 KeV/micron carbon !



Modelling hypoxia in TPS

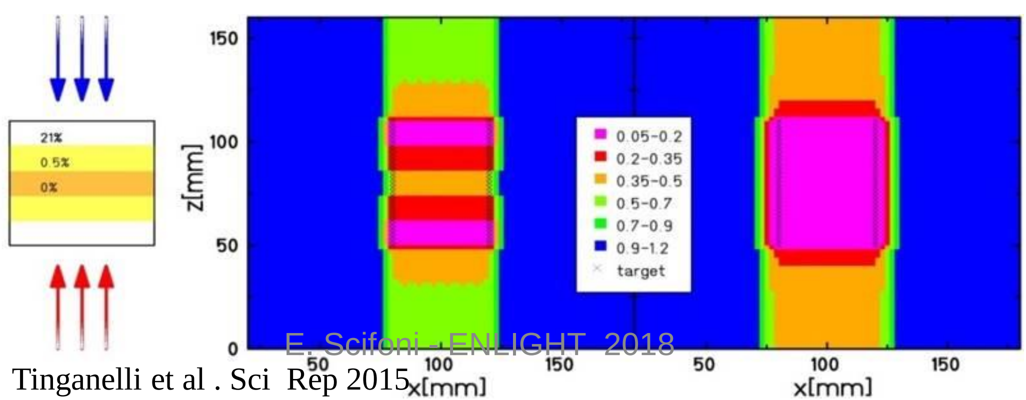




Horsman et al
Nat. Rev. Clin. Oncol. (2012)

LET and dose distribution of the particle fields automatically adjusted from the optimization to the oxygen distribution

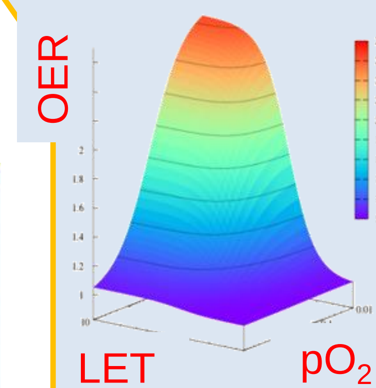
Courtesy of E. Scifoni



Tinganelli et al . Sci Rep 2015

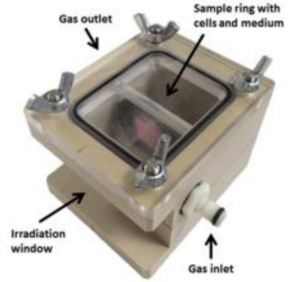
Semi-empirical model for $OER(pO_2, LET)$

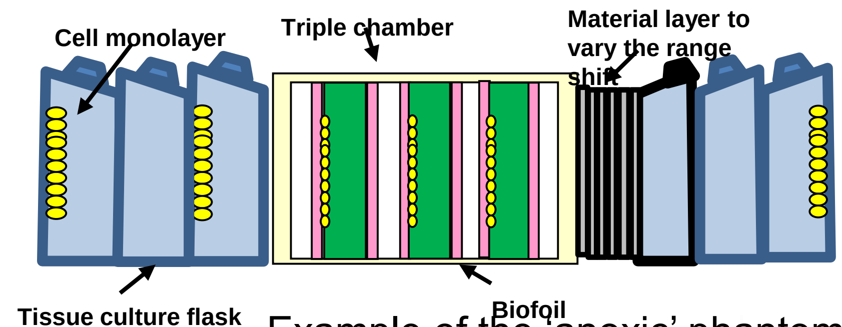
Scifoni et al . Phys Med Biol 2013



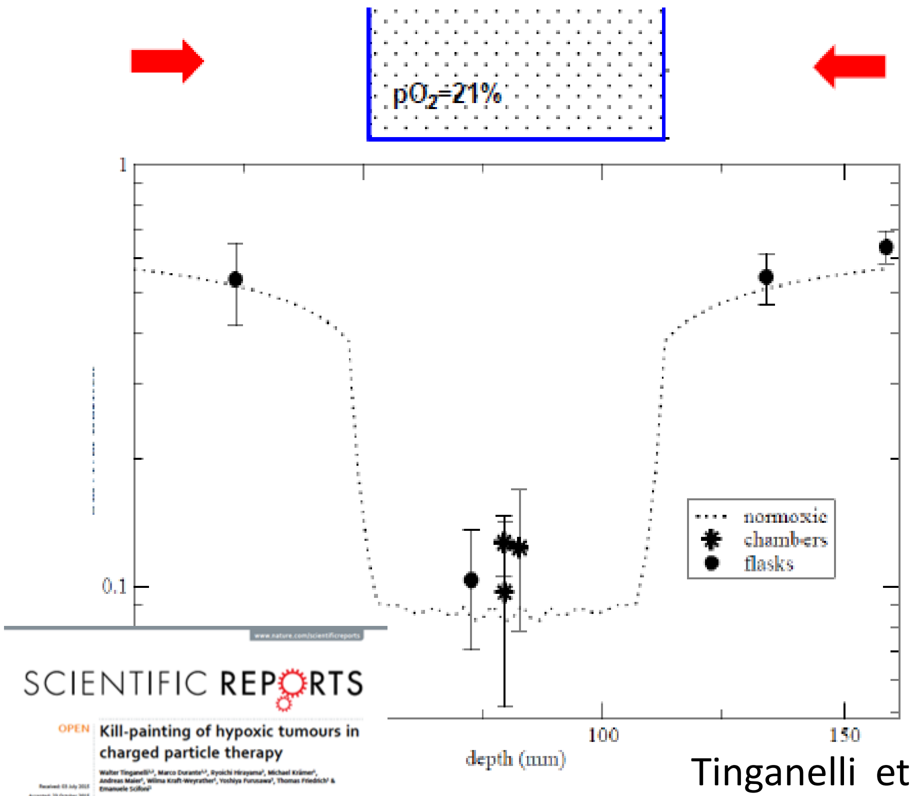
Experimental verification: Hypoxic cell chambers

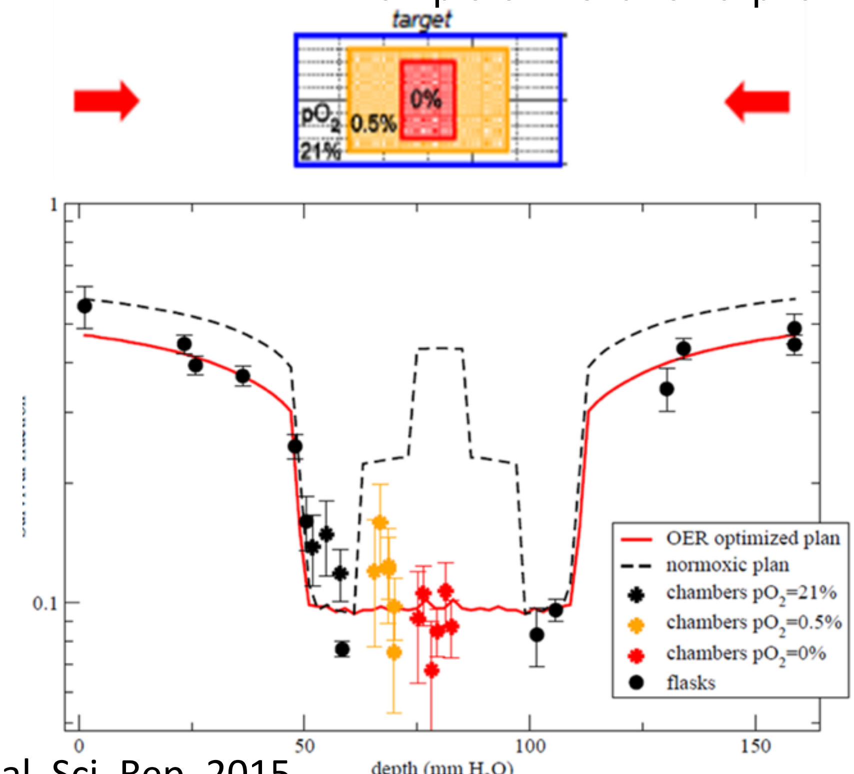
2 Fields C ions@GSI





Example of the 'anoxic' phantom





Tinganelli et al. Sci. Rep. 2015.

Courtesy of E. Scifoni

Hypoxia

Normal tissue pO2 40 – 60 mmHg

pO2 < 10 mmHg hypoxia

pO2 < 3 mmHg severe

Tatum et al., (2006)'Hypoxia: Importance in tumor biology, noninvasive measurement by imaging, and value of its measurement in the management of cancer therapy', International Journal of Radiation Biology,82:10,699 — 757

Human cancers are hypoxic

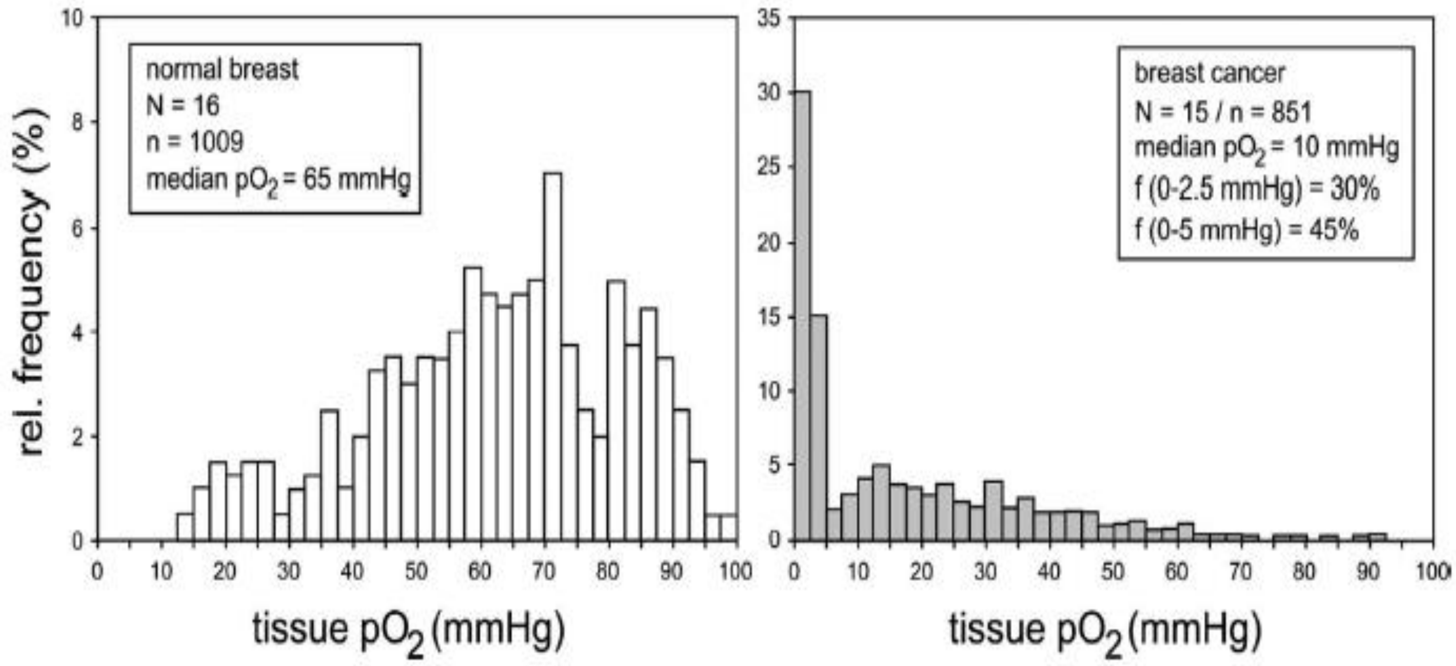


Figure 3. Frequency distribution (histogram) of measured pO_2 values in normal breast tissue (left) and in locally advanced breast cancers (right). N, number of patients investigated; n, number of pO_2 values measured; f(0 – 2.5 mm Hg), fraction of pO_2 values between 0 and 2.5 mm Hg; f(0 – 5 mm Hg), fraction of pO_2 values between 0 and 5 mm Hg (adapted from Vaupel et al. 2002).

Only very smal tumors are not hypoxic

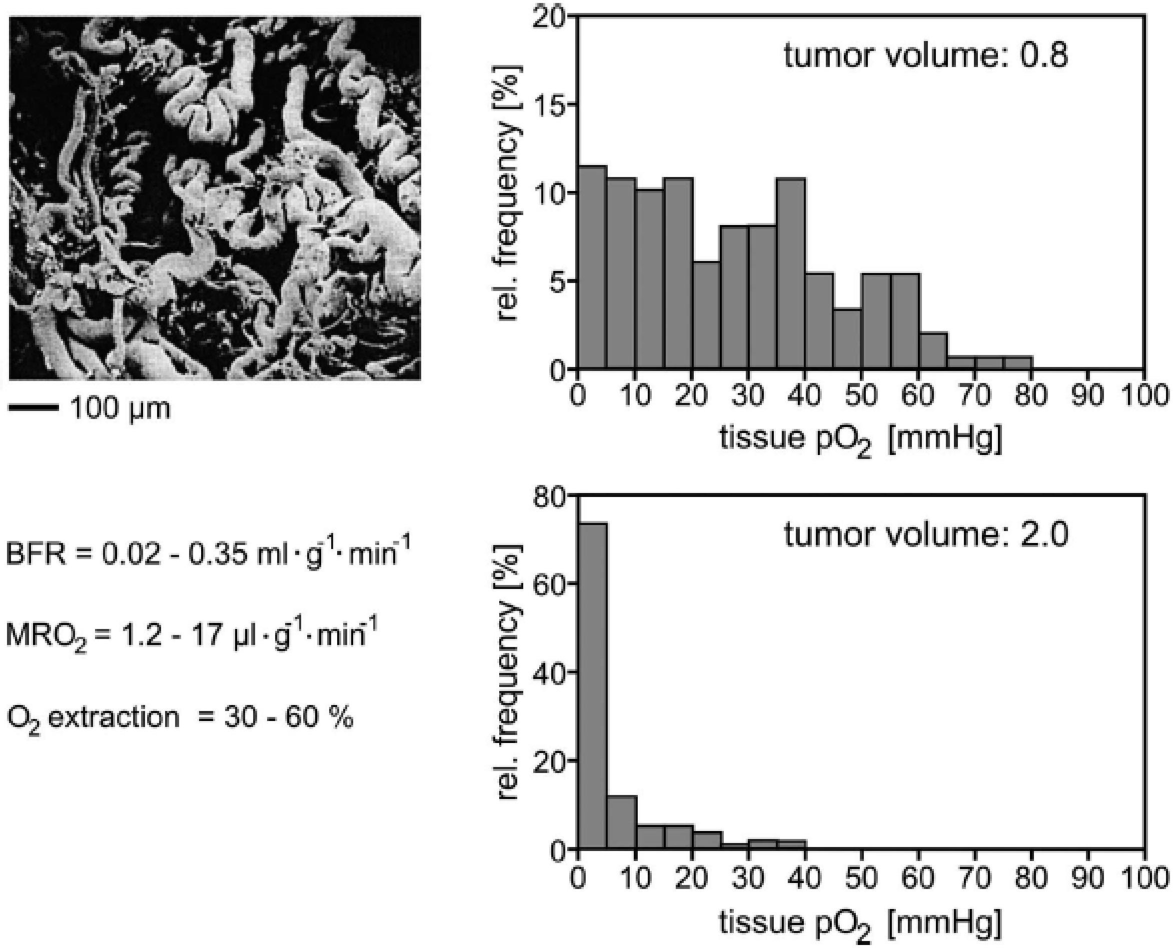
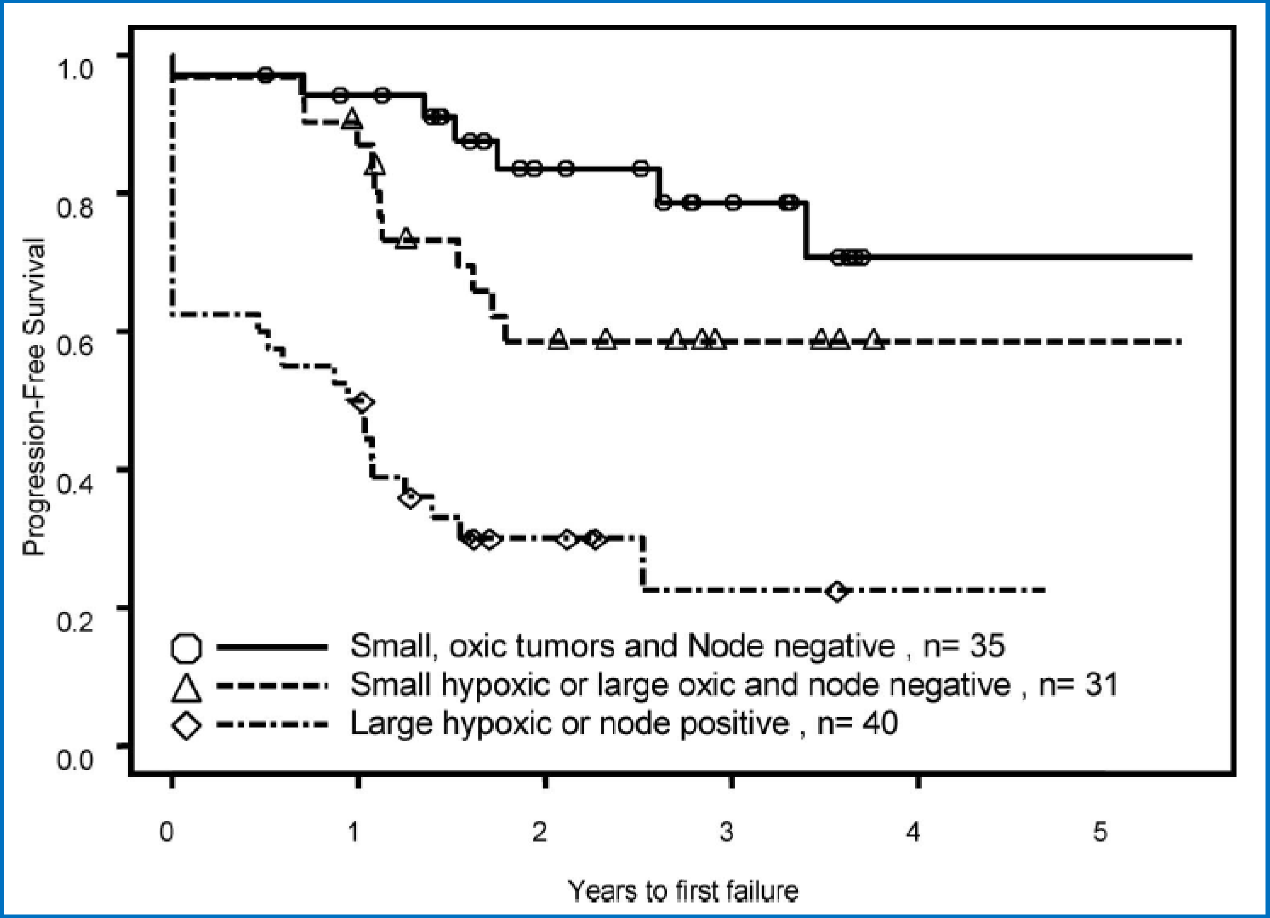


Figure 4. Microvascular pattern (upper left) and pO_2 histograms for small (upper right) and large rat DS-sarcomas (lower right). Blood flow rate (BFR), oxygen consumption rate (MRO_2), and oxygen extraction in experimental rat tumors are greatly volume dependent (adapted from Vaupel et al. 2003).

Hypoxia is an interesting subject



Cervical cancer survival dependso on tumor hypoxia (polarographic Eppendorf needle electrode measurments)

Fyles et al. JCO 2003

cancers

MDPI

Review

Cyclic Hypoxia: An Update on Its Characteristics, Methods to Measure It and Biological Implications in Cancer

Samuel B. Bader [1], Mark W. Dewhirst [2,*] and Ester M. Hammond [1,*]

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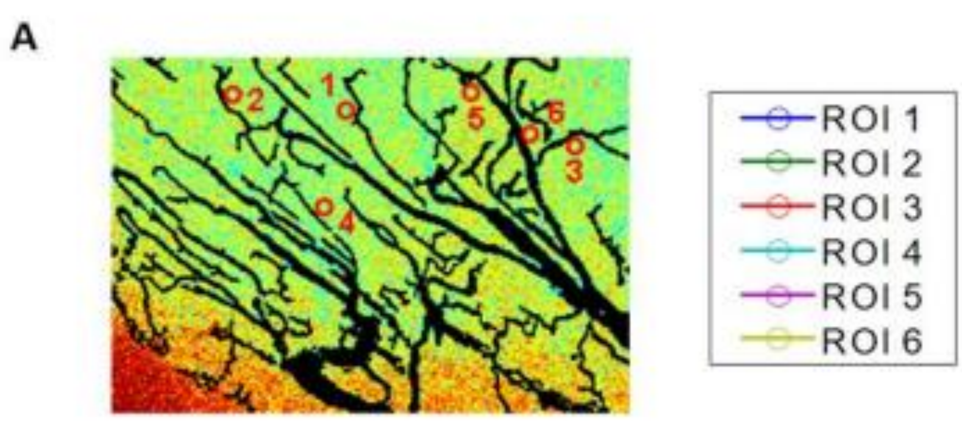
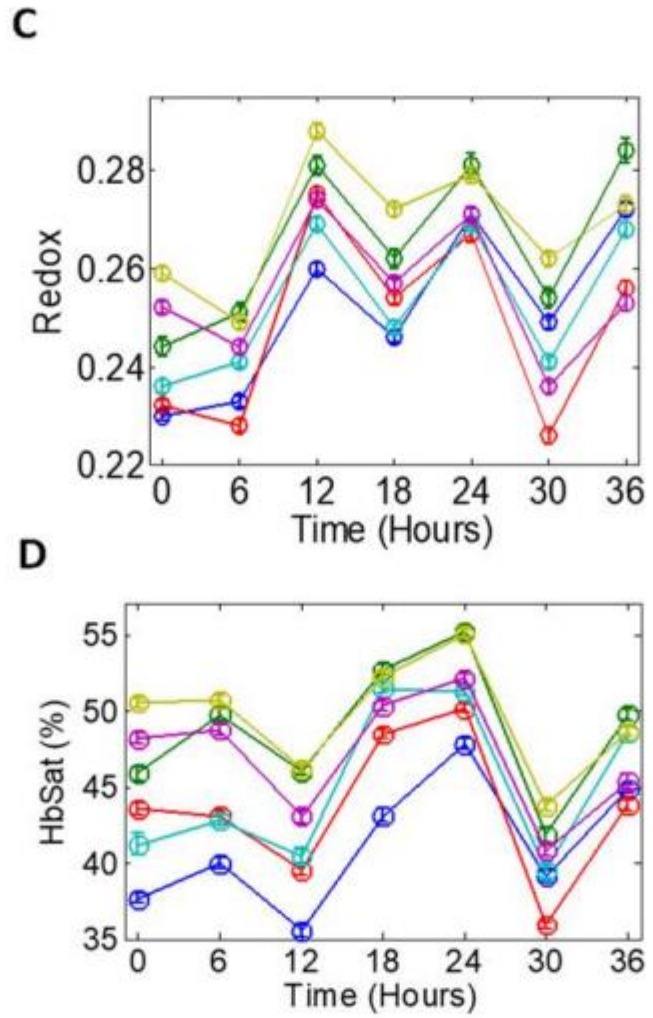
2 Radiation Oncology Department, Duke University School of Medicine, Durham, NC 27710, U
* Correspondence: mark.dewhirst@duke.edu (M.W.D.); ester.hammond@oncology.ox.ac.uk (E



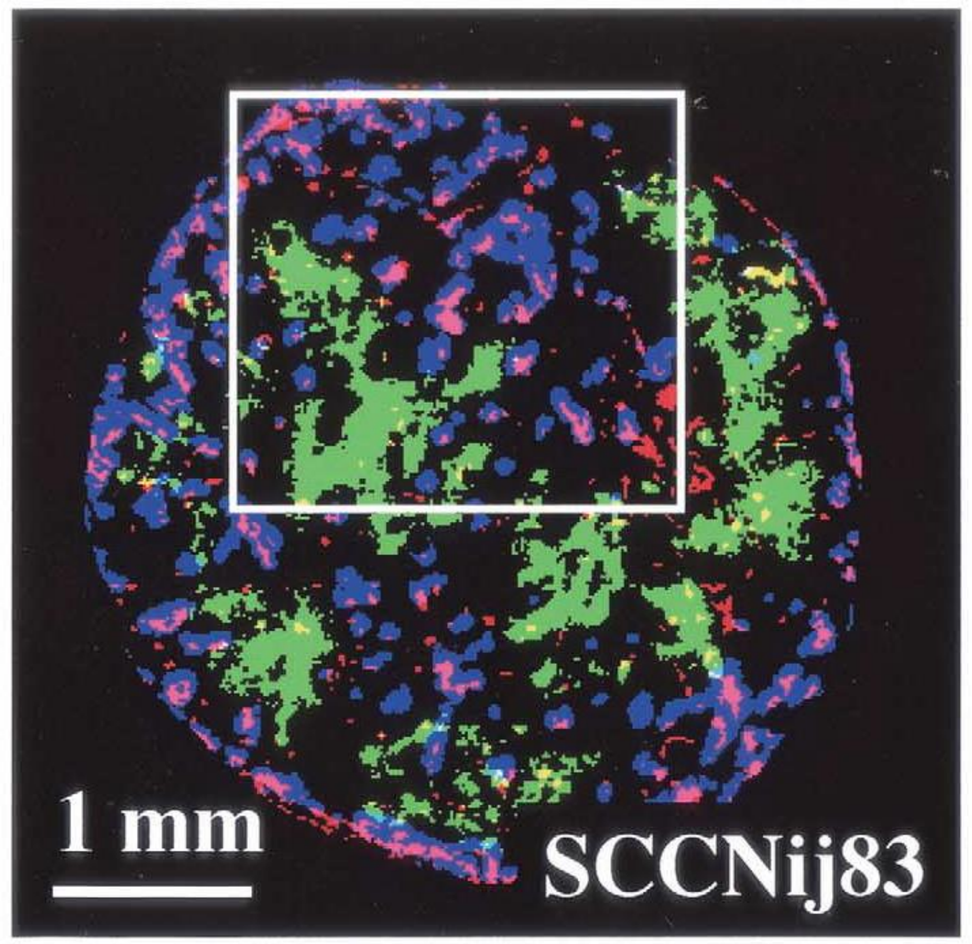


Two favourable characteristics

1. Hypoxia is a microenvironment property (not a single cell one)

2. Hypoxia can be measured

Microenvironment



Hypoxic areas in human cells (pimonidazole) are green, and mouse endothelium is red. Perfused zones (Hoechst 33342) are blue, and vascular structures in these zones are pink

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 54, No. 1, pp. 215–228, 2002

0360-3016/02/$–see front matter

PII S0360-3016(02)02938-3

BIOLOGY CONTRIBUTION

VASCULAR ARCHITECTURE, HYPOXIA, AND PROLIFERATION IN FIRST-GENERATION XENOGRAFTS OF HUMAN HEAD-AND-NECK SQUAMOUS CELL CARCINOMAS

Anna S.E. Ljungkvist, M.Sc.,*† Johan Bussink, M.D., Ph.D.,* Paulus F.J.W. Rijken, M.Sc.,* Johannes H.A.M. Kaanders, M.D., Ph.D.,* Albert J. van der Kogel, Ph.D.,* and Juliana Denekamp, Ph.D., D.Sc.†

Measuring hypoxia

- polarographic needle electrodes
- PET

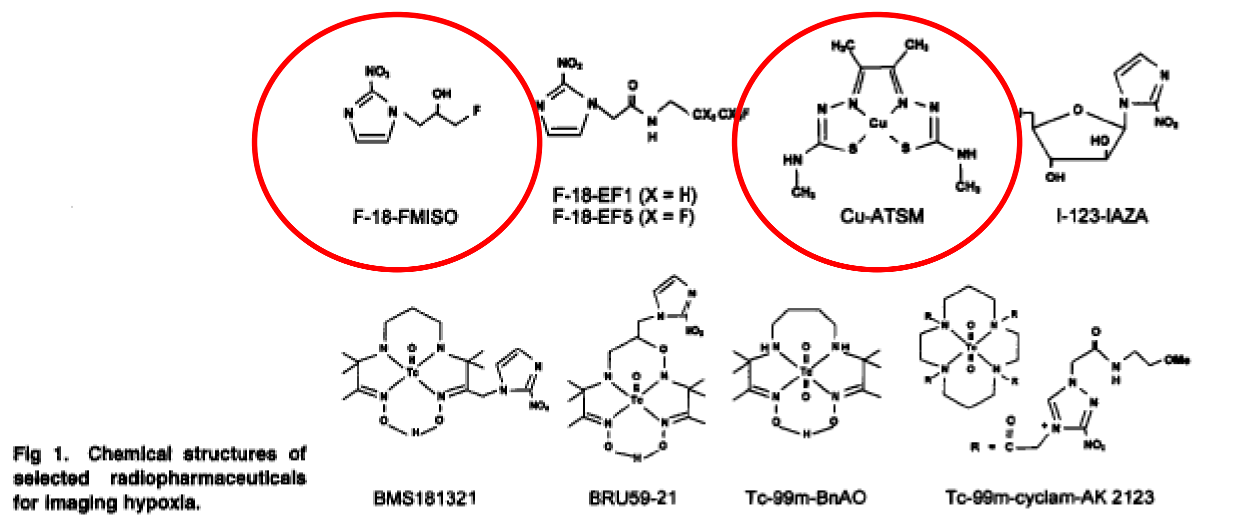
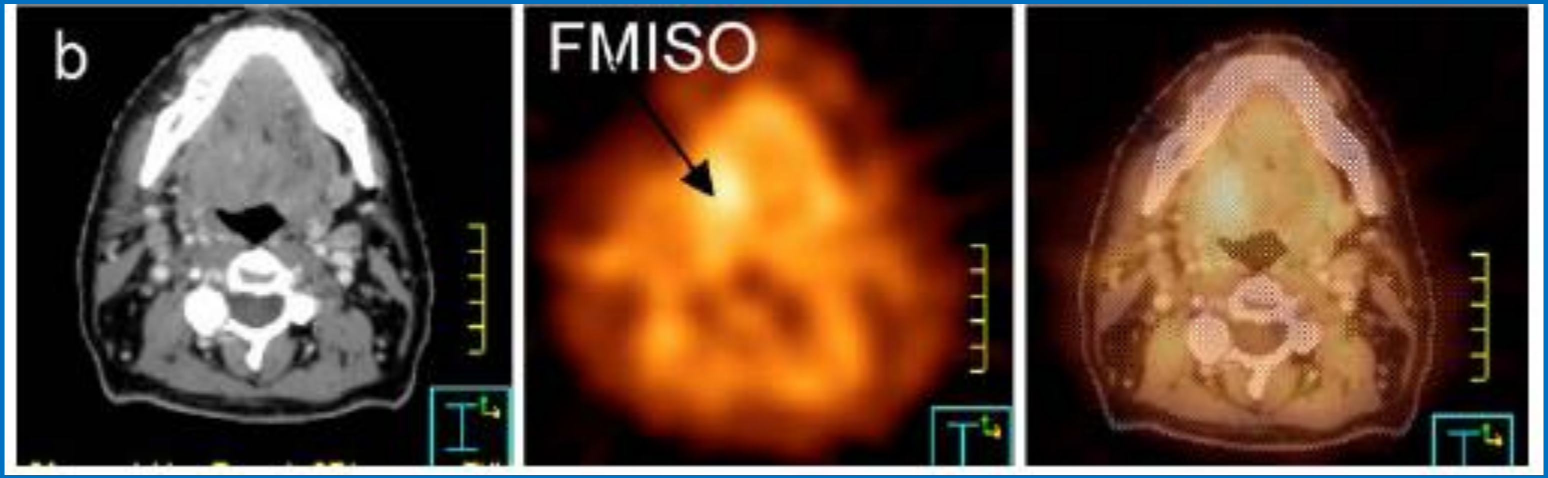


Fig 1. Chemical structures of selected radiopharmaceuticals for imaging hypoxia.

18F-MISO

- First reduction only inside living cells, if pO2> 20 mmHg there is a immediate re-oxidation, otherwise there is a second reduction and the drug can bind to nmacromolecules and accumulate within the cell
- Easy to produce and ship

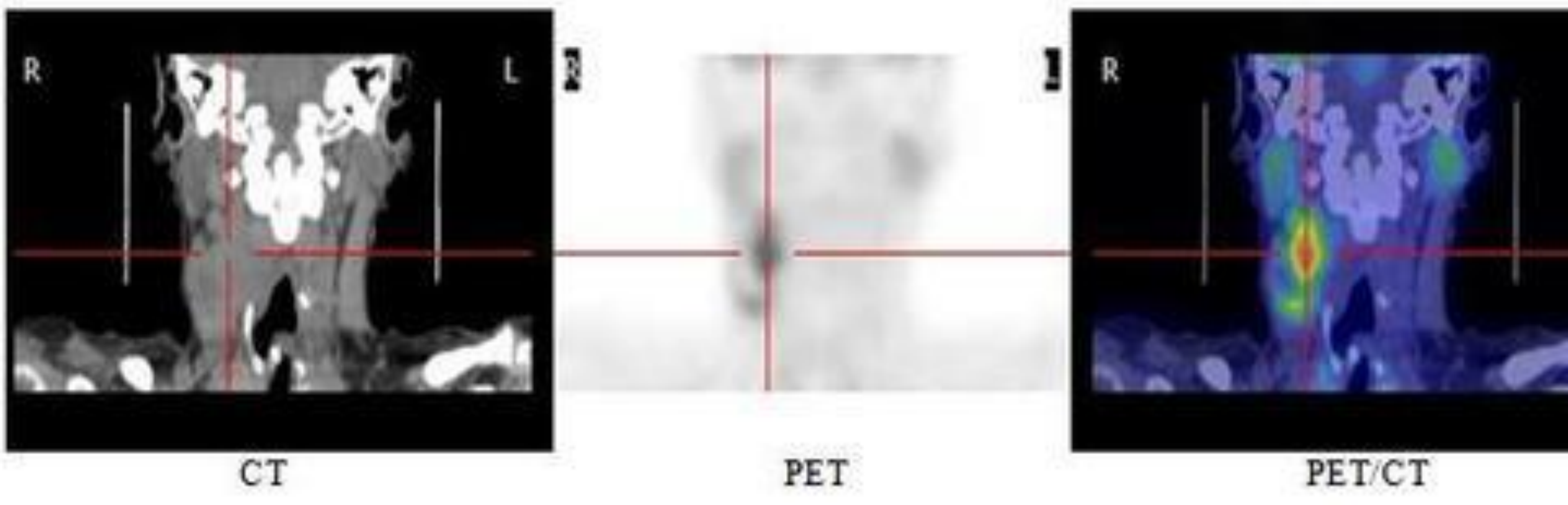
Sub-optimal contrast



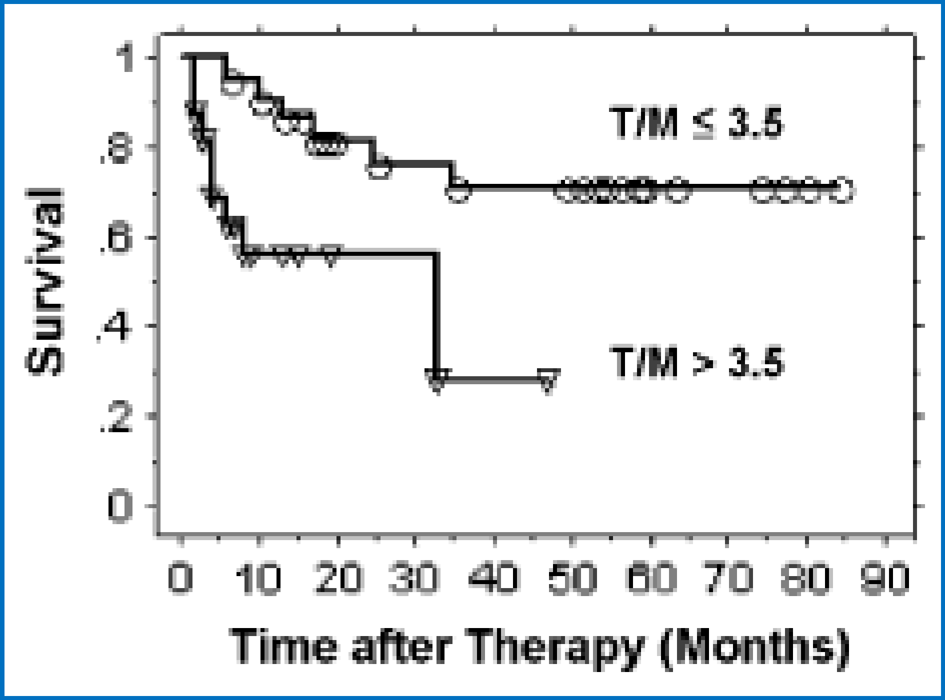
Cu-ATSM

- First reduction only inside living cells (NADH is needed)
- Second reduction only if low pO2
- Good contrast
- Radioactive Cu is more difficult to produce: Cu60 half life 24 min

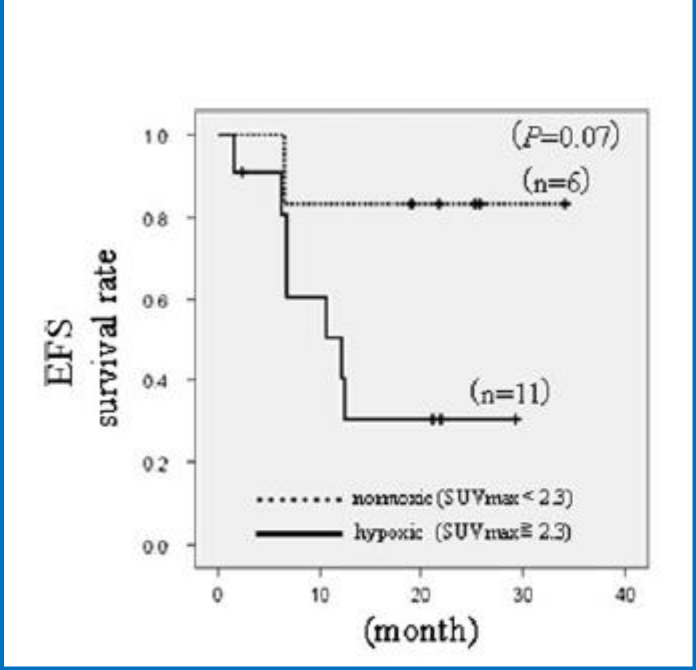
Better contrast with Cu-ATSM

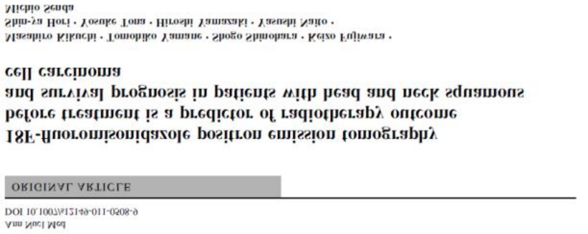


Hypoxia measured with Cu-ATSM PET is still predictive of survival in cervical cancer



Hypoxia measured with F-miso PET is predictive of outcome in head and neck cancer

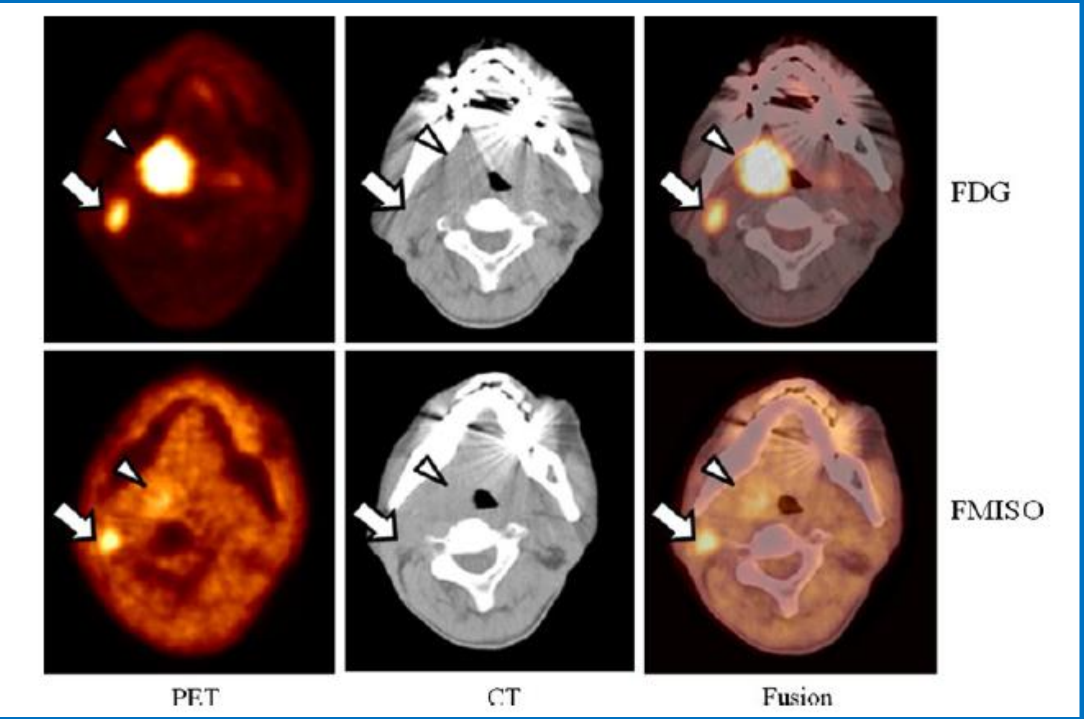



Ann Nucl Med
DOI 10.1007/s12149-011-0508-9

ORIGINAL ARTICLE

18F-fluoromisonidazole positron emission tomography before treatment is a predictor of radiotherapy outcome and survival prognosis in patients with head and neck squamous cell carcinoma

Masahiro Kikuchi · Tomohiko Yamane · Shogo Shinohara · Keizo Fujiwara · Shin-ya Hori · Yosuke Tona · Hiroshi Yamazaki · Yasushi Naito · Michio Senda



Static or kinetic PET measurements?

INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **50** (2005) 2209–2224 doi:10.1088/0031-9155/50/10/002

A kinetic model for dynamic [^{18}F]-Fmiso PET data to analyse tumour hypoxia

Daniela Thorwarth[1], **Susanne M Eschmann**[2], **Frank Paulsen**[3] **and Markus Alber**[1]

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[2] Department of Nuclear Medicine, Radiological University Clinic, Otfried-Müller-Str. 14, 72076 Tübingen, Germany
[3] Department of Radiation Therapy, University Hospital for Radiation Oncology, Hoppe-Seyler-Str. 3, 72076 Tübingen, Germany

TAC (Time Activity Curves) are created

A kinetic model to analyse tumour hypoxia

Table 1. Table of acquired image frames for each patient ($n = 16$).

Time p.i. (min)	0–2	2–4	4–15	15–60	120	180	240
Acquisition time	12 × 10 s	8 × 15 s	11 × 60 s	9 × 5 min	1 × 5 min	1 × 8–9 min	1 × 10–12 min
Patient no.							
1, 4	×	×	×	×	×	×	×
3, 5, 7, 9, 10, 12, 13, 15	×	×	×	–	×	–	×
8	×	×	×	–	×	×	×
11, 16	×	×	×	×	×	–	×
2, 14	×	×	×	3 × 5 min	×	–	×
6	×	×	×	5 × 5 min	×	–	×

One F-miso injection, multiple data acquisition over time

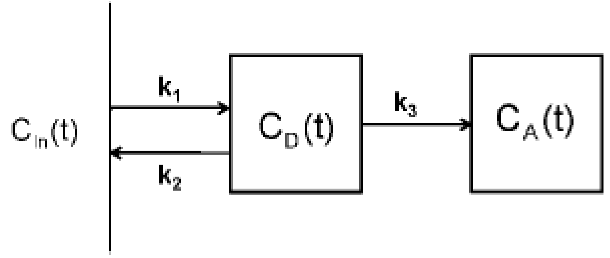
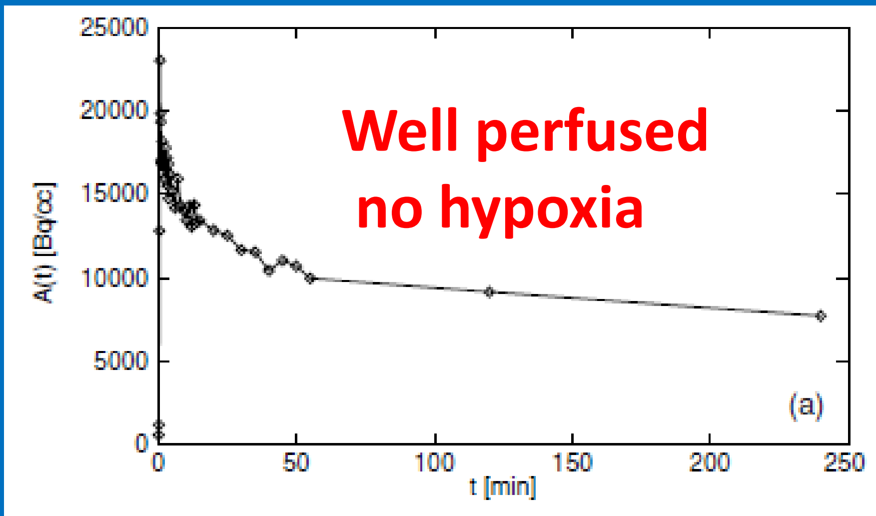


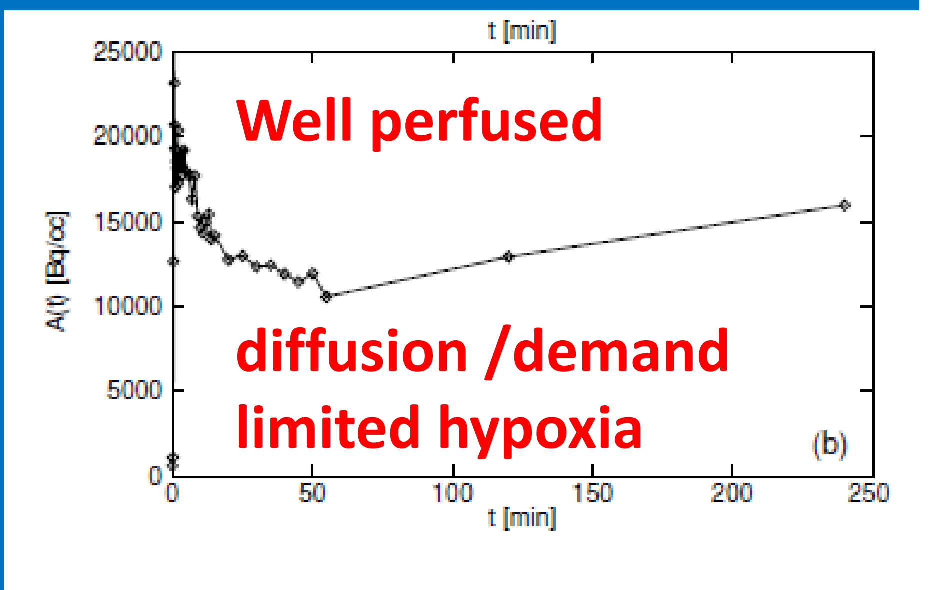
Figure 1. Compartmental model consisting of a diffusive and an accumulative compartment. The input function $C_{\mathrm{In}}(t)$ comprises the tracer concentration in the blood and in the interstitial space close to the vessels.

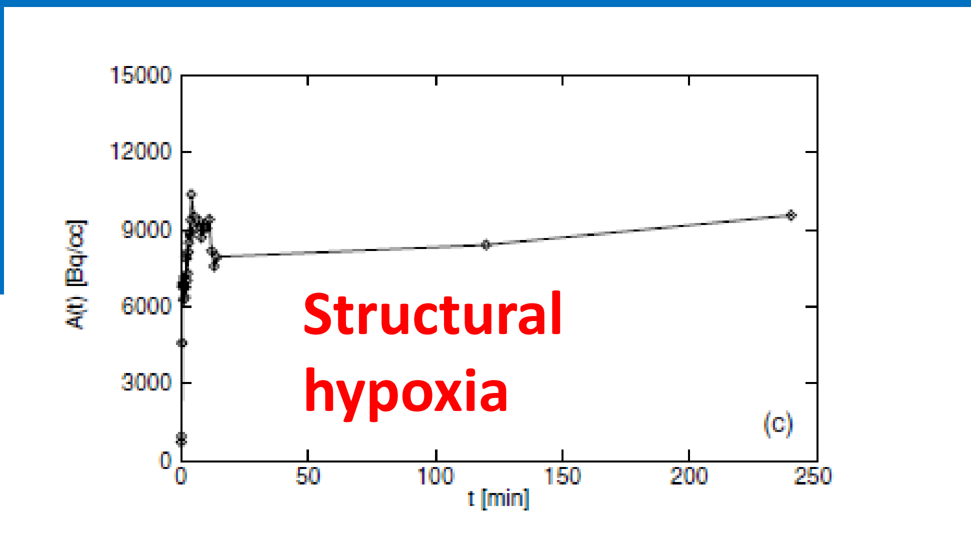
$$\frac{\partial}{\partial t} C_D(t) = k_1 C_{\mathrm{In}}(t) - (k_2 + k_3) C_D(t)$$
$$\frac{\partial}{\partial t} C_A(t) = k_3 C_D(t).$$

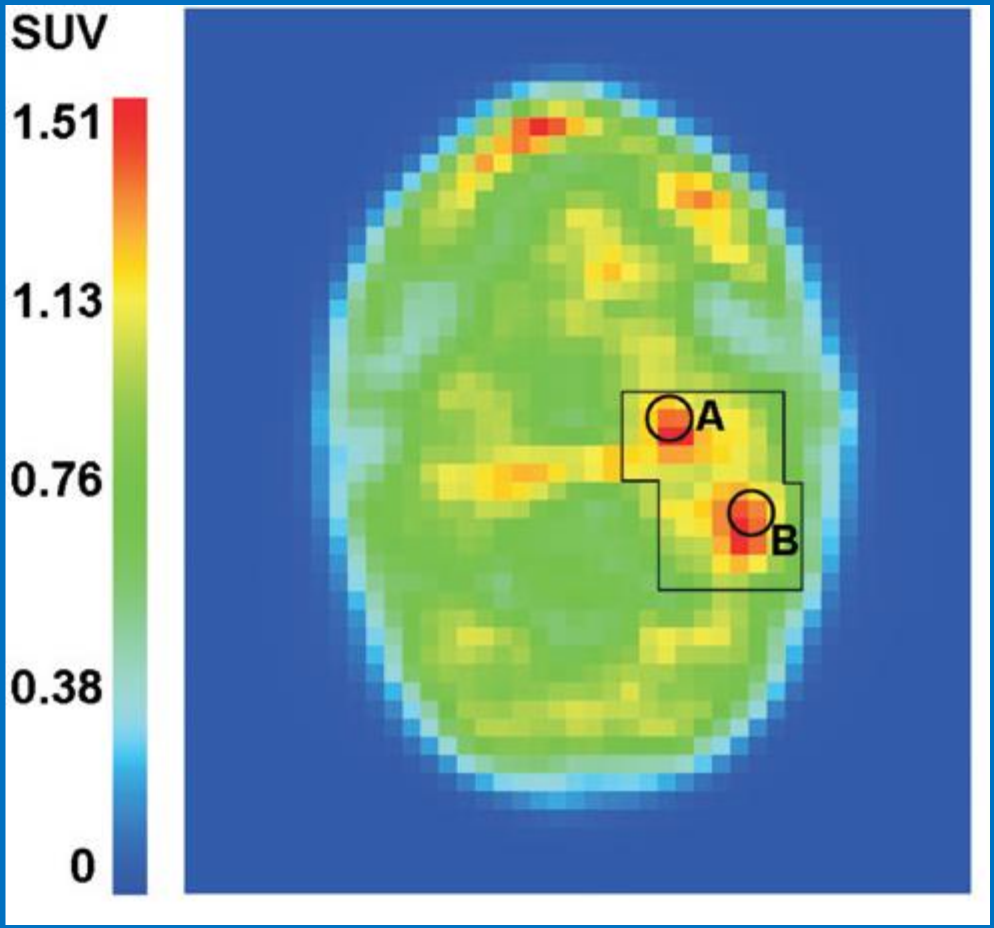
$$S(t) = w_0 C_{\mathrm{In}}(t) + \tilde{w}_D \int_0^t \mathrm{e}^{-\tilde{k}_3(t-\tau)} C_{\mathrm{In}}(\tau)\,\mathrm{d}\tau + \tilde{w}_A \int_0^t (1 - \mathrm{e}^{-\tilde{k}_3(t-\tau)}) C_{\mathrm{In}}(\tau)\,\mathrm{d}\tau.$$

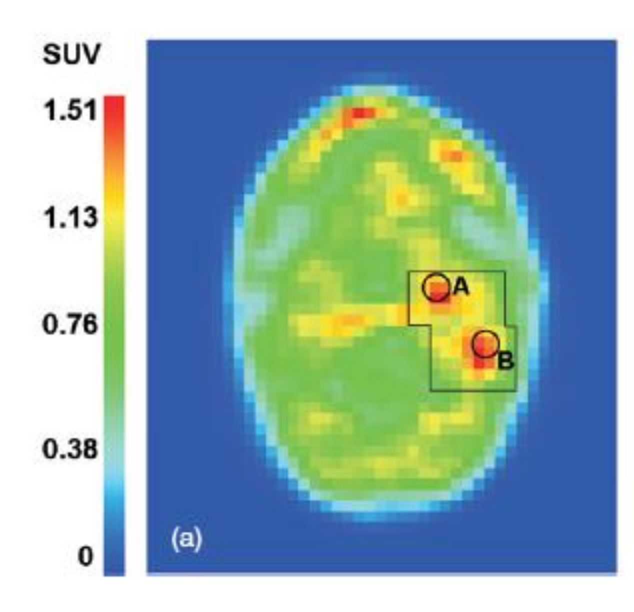
Three patterns

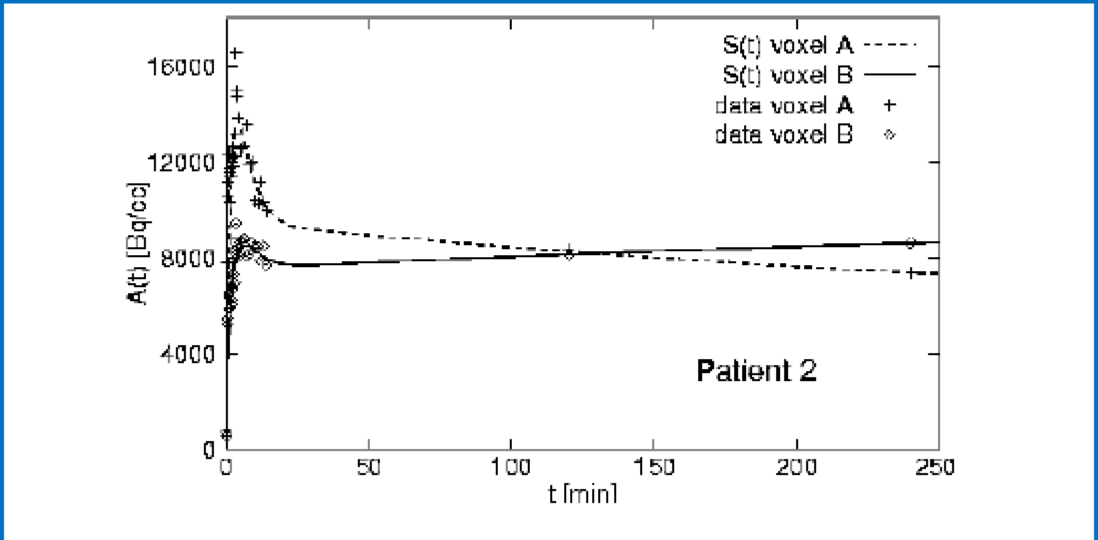




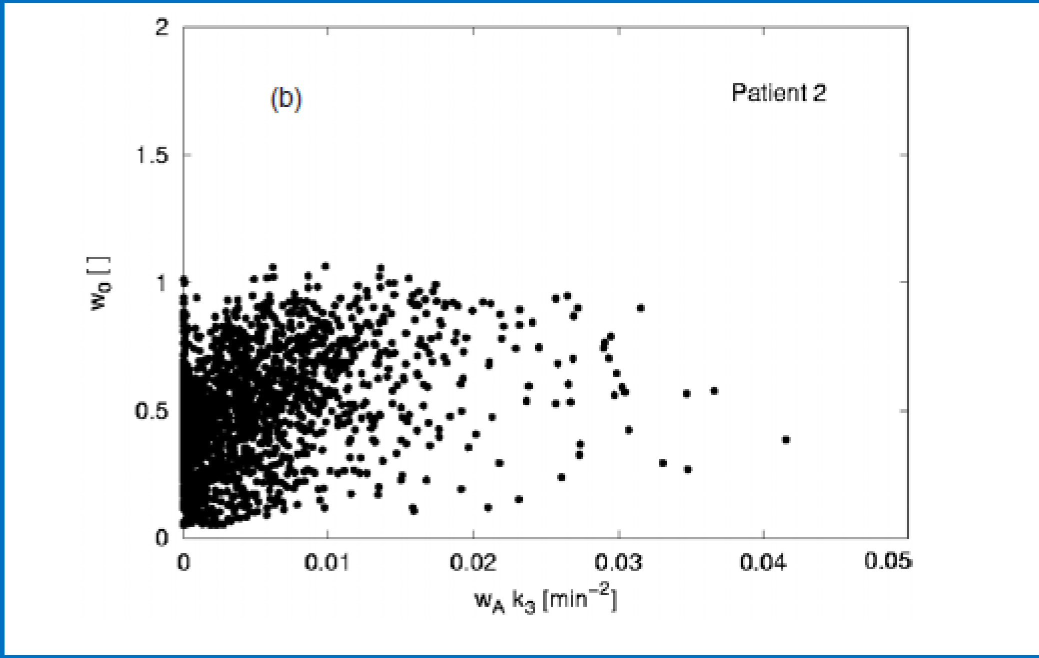



SUV
1.51
1.13
0.76
0.38
0
A
B


SUV
1.51
1.13
0.76
0.38
0
A
B
(a)


S(t) voxel A
S(t) voxel B
data voxel A
data voxel B
A(t) [Bq/cc]
16000
12000
8000
4000
0
0
50
100
150
200
250
t [min]
Patient 2

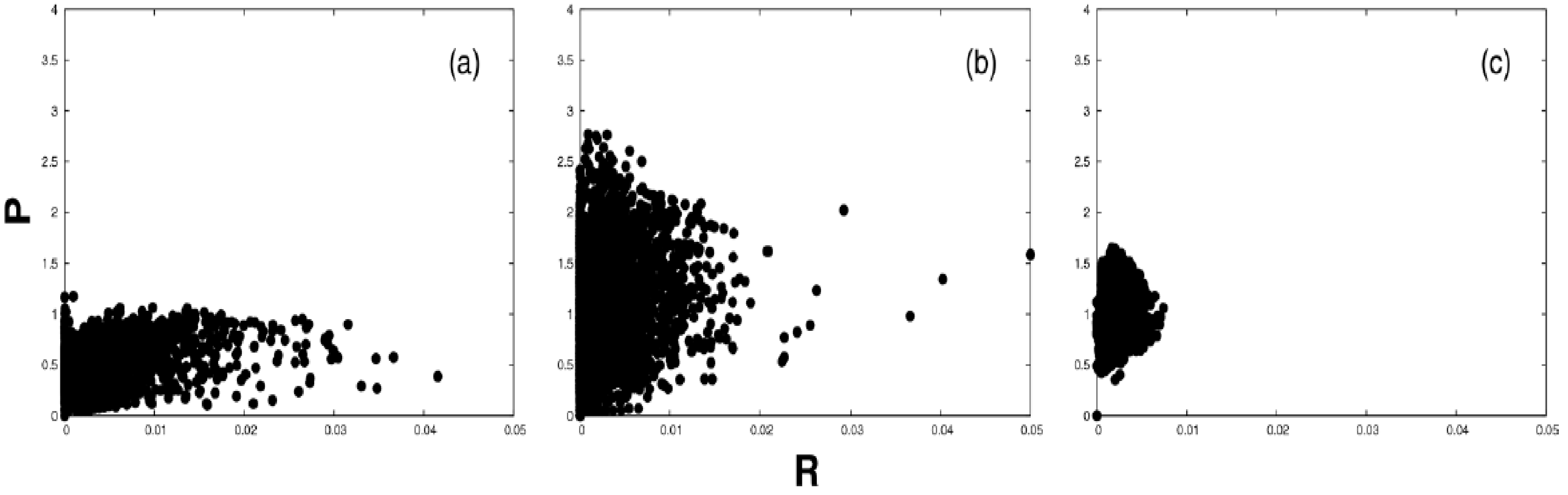
Scatter plots



W_0 describes how fast the radiodrug goes from the blood to the interstitial fluid

$W_a k_3$ describes how fast it is trapped in hypoxic cells

Three kinds of tumors:

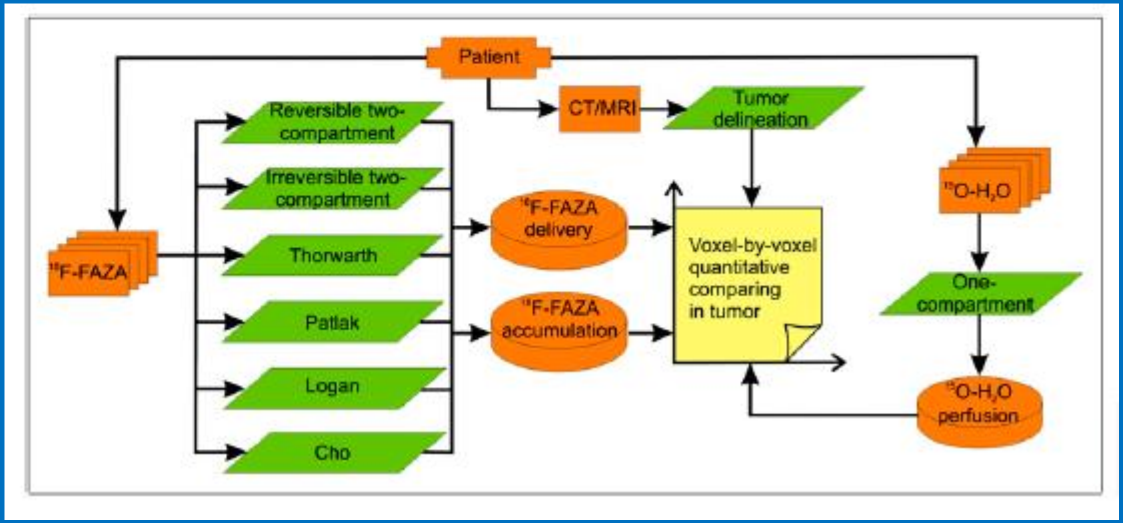


a) hypoxic because of poor blood supply
b) Hypoxic despite good blood supply (increased consumption ?)
c) Well oxygenated

Quantitative Assessment of Hypoxia Kinetic Models by a Cross-Study of Dynamic ^{18}F-FAZA and ^{15}O-H_2O in Patients with Head and Neck Tumors

Kuangyu Shi[1], Michael Souvatzoglou[2], Sabrina T. Astner[1], Peter Vaupel[1], Fridtjof Nüsslin[1], Jan J. Wilkens[1], and Sibylle I. Ziegler[2]

[1]*Department of Radiotherapy and Radiooncology, Klinikum rechts der Isar, Technische Universität München, Munich, Germany;* and [2]*Department of Nuclear Medicine, Klinikum rechts der Isar, Technische Universität München, Munich, Germany*

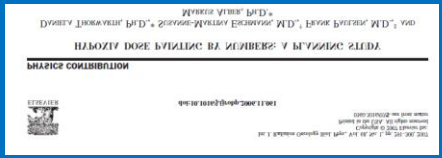


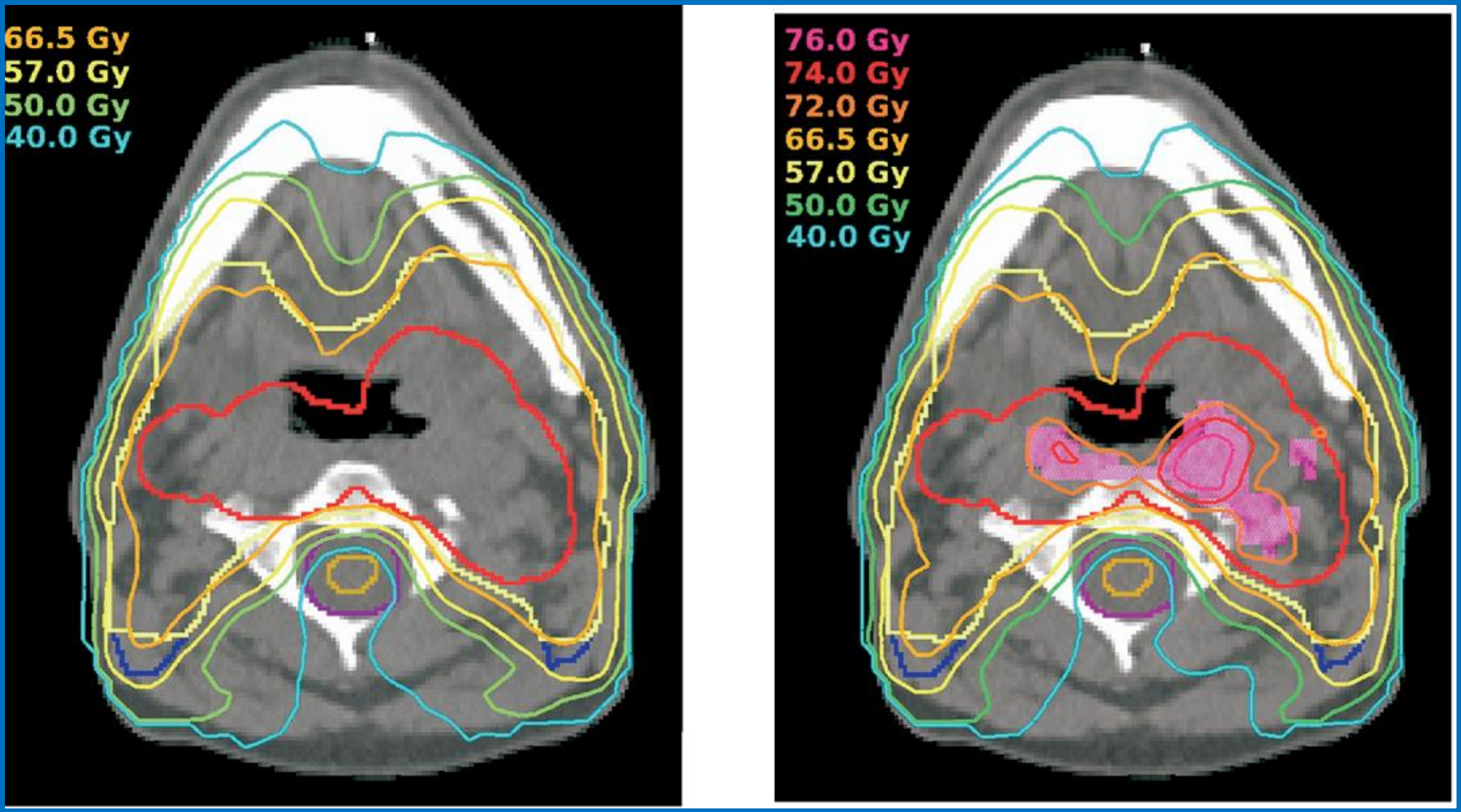
Although kinetic modeling has advantages over static assessment (*21*), the behavior varies greatly for different models of hypoxia evaluation. Different models even lead to opposite interpretations in some situations.

Dose escalation for hypoxic tumors

- More dose to the tumor (uniform dose escalation)
- More dose to the hypoxic part of the tumor (dose painting by contours DPBC)
- The more it is hypoxic the higher the dose (Dose Painting By Numbers DPBN)

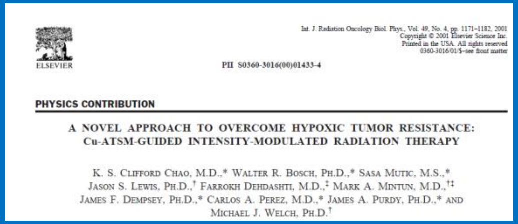
Uniform dose escalation





Hypoxia information is used only to decide weather or not to give an additional 6 Gy (70 → 76) the volume is decided indipendently (e.g. FDG - PET)

Dose painting by contours (1)


Int. J. Radiation Oncology Biol. Phys., Vol. 49, No. 4, pp. 1171–1182, 2001
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0360-3016/01/$–see front matter

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PII S0360-3016(00)01433-4

PHYSICS CONTRIBUTION

A NOVEL APPROACH TO OVERCOME HYPOXIC TUMOR RESISTANCE: Cu-ATSM-GUIDED INTENSITY-MODULATED RADIATION THERAPY

K. S. Clifford Chao, M.D.,* Walter R. Bosch, Ph.D.,* Sasa Mutic, M.S.,* Jason S. Lewis, Ph.D.,† Farrokh Dehdashti, M.D.,‡ Mark A. Mintun, M.D.,†‡ James F. Dempsey, Ph.D.,* Carlos A. Perez, M.D.,* James A. Purdy, Ph.D.,* and Michael J. Welch, Ph.D.†

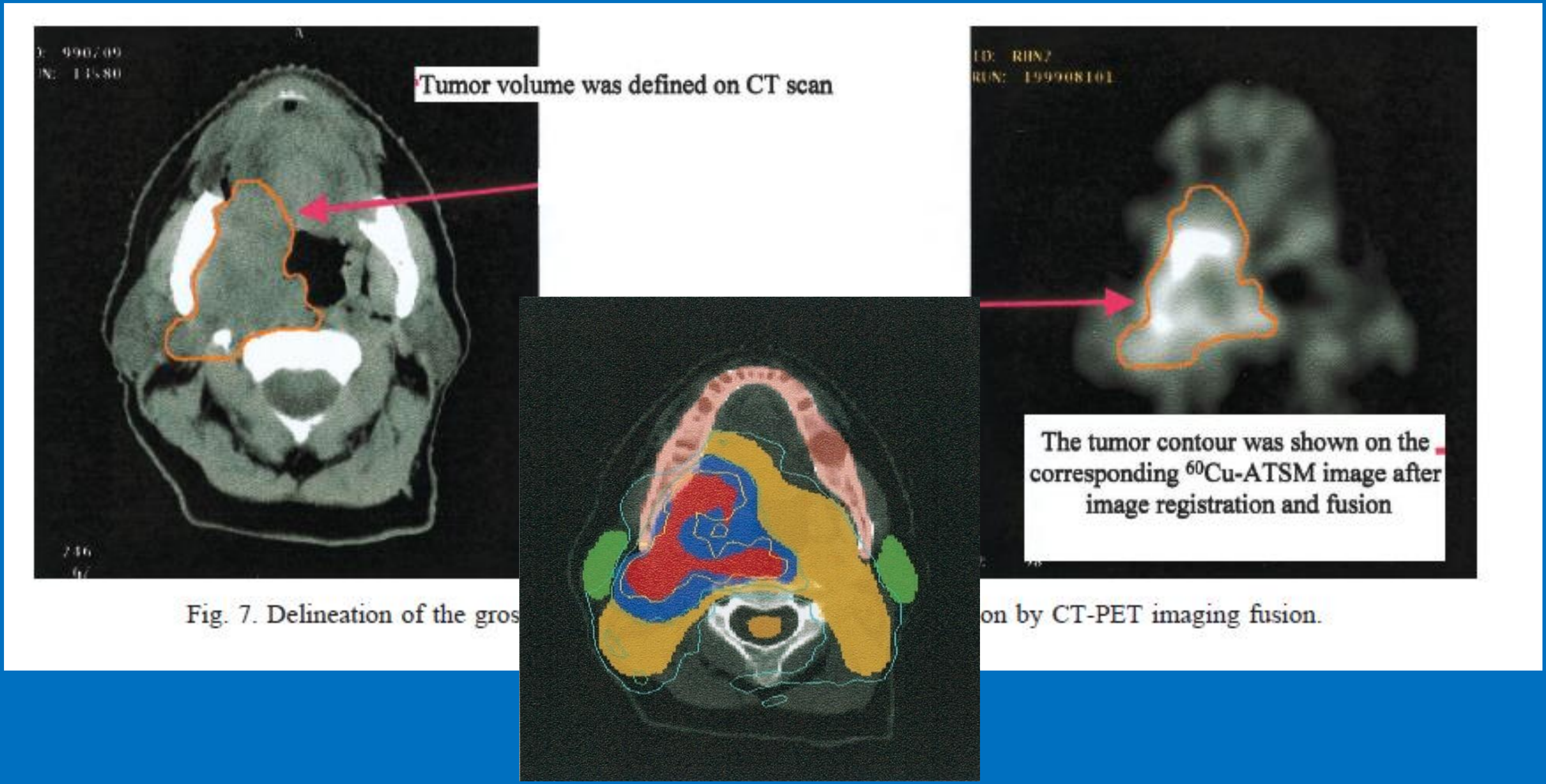
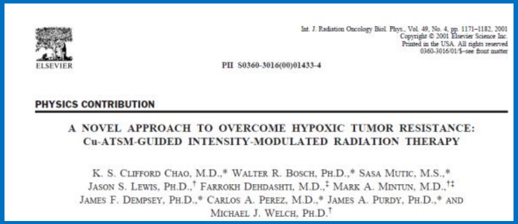


Fig. 7. Delineation of the gros ... on by CT-PET imaging fusion.

All the volume with drug uptake (Cu-ATSM) over a threshold receives the boost (80 Gy vs. 70 Gy)

Dose painting by numbers

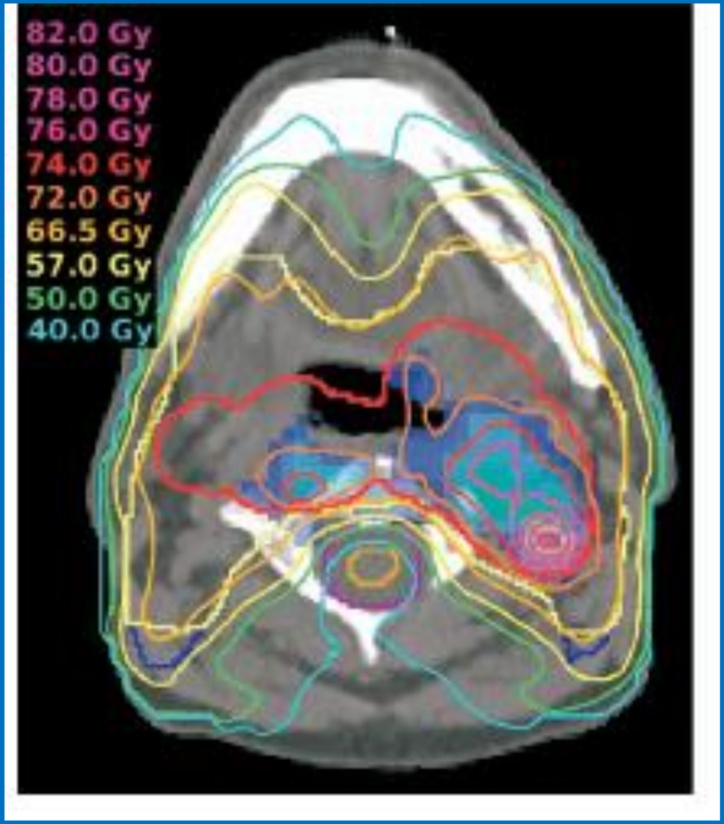

ELSEVIER
Int. J. Radiation Oncology Biol. Phys., Vol. 49, No. 4, pp. 1171–1182, 2001

0360-3016/01/$–see front matter
PII S0360-3016(00)01433-4

PHYSICS CONTRIBUTION

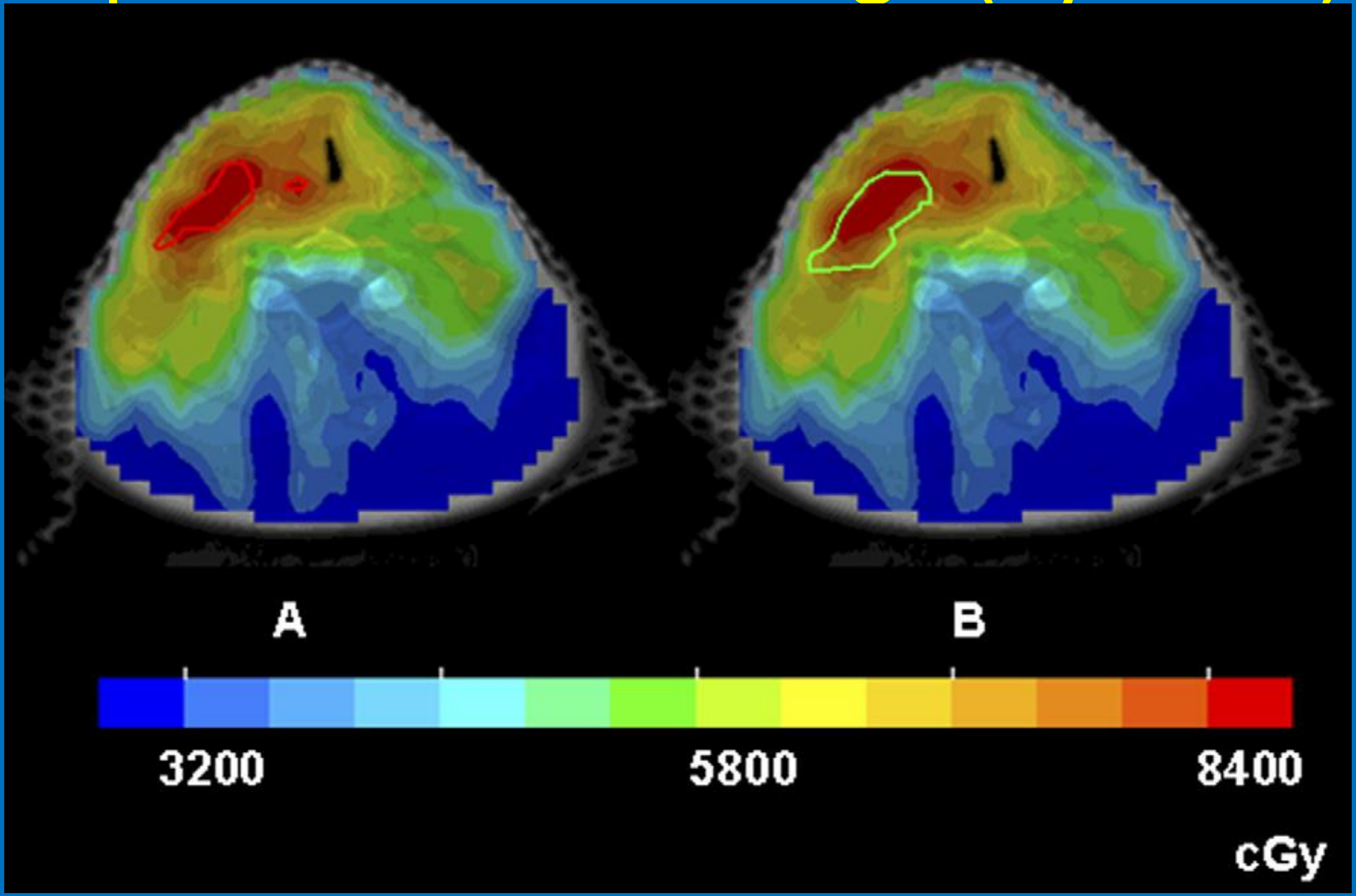
A NOVEL APPROACH TO OVERCOME HYPOXIC TUMOR RESISTANCE: Cu-ATSM-GUIDED INTENSITY-MODULATED RADIATION THERAPY

K. S. Clifford Chao, M.D.,* Walter R. Bosch, Ph.D.,* Sasa Mutic, M.S.,* Jason S. Lewis, Ph.D.,† Farrokh Dehdashti, M.D.,‡ Mark A. Mintun, M.D.,†‡ James F. Dempsey, Ph.D.,* Carlos A. Perez, M.D.,* James A. Purdy, Ph.D.,* and Michael J. Welch, Ph.D.†



More drug (F-Miso)
more hypoxia
more dose

Hipoxic volume change (by itself)



Lin et al. IJROBP 2008

Hypoxic volume changes, thanks to RT

- It would be desiderable to describe the change of hypoxia and possibly the influence of RT on reoxygenation.
- Multiple PET over the RT treatment duration would be necessary

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 2, pp. 515–521, 2007

0360-3016/07/$–see front matter

doi:10.1016/j.ijrobp.2006.12.037

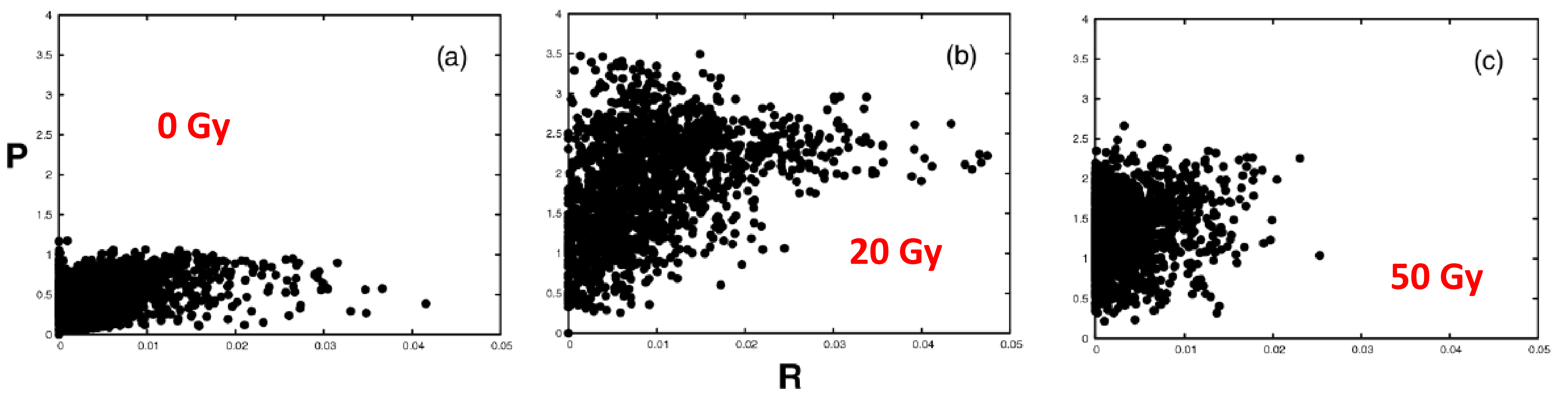
PHYSICS CONTRIBUTION

A MODEL OF REOXYGENATION DYNAMICS OF HEAD-AND-NECK TUMORS BASED ON SERIAL 18F-FLUOROMISONIDAZOLE POSITRON EMISSION TOMOGRAPHY INVESTIGATIONS

DANIELA THORWARTH, PH.D.,* SUSANNE-MARTINA ESCHMANN, M.D.,[†] FRANK PAULSEN, M.D.,[‡] AND MARKUS ALBER, PH.D.*

Only 15 HN patients, serial F-Miso (dynamic) PET: at least at 0 and 20 Gy, for some patients also at 50 Gy and 70 Gy

How do perfusion and retention change during therapy ? (according to Thorwarth model)

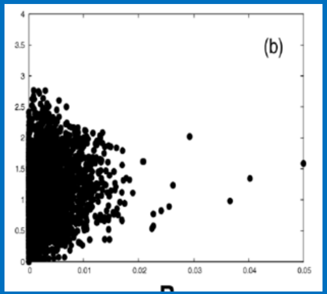


Inflammation ?

reoxigenation

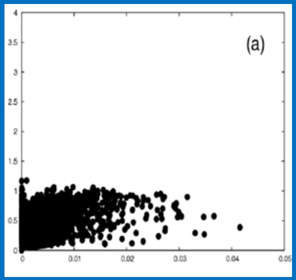
What is the mechanism of reoxygenation ?

- Reduced consumption of stunned tumor cells
- Increased perfusion due to inflammation



fast

- Tumor shrinkage



slow

How much dose escalation ?

- Arbitrary : 70 Gy → 80 Gy
- Based on TCP model :

$$DEF_i = \frac{\alpha_0 D_0}{\alpha_0 D_0 - \ln(M_i)} = \frac{\alpha_0}{\alpha_i}.$$

M being the excess number of live cell in a voxel due to hypoxia

ELSEVIER
Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 1, pp. 291–300, 2007

0360-3016/07/$–see front matter
doi:10.1016/j.ijrobp.2006.11.061

PHYSICS CONTRIBUTION

HYPOXIA DOSE PAINTING BY NUMBERS: A PLANNING STUDY

Daniela Thorwarth, Ph.D.,* Susanne-Martina Eschmann, M.D.,† Frank Paulsen, M.D.,‡ and Markus Alber, Ph.D.*

Sooner or later ?

- Appling dose escalation after the re-oxygenation has taken place might be more efficient as you do not ‘waste’ precious extra dose in the initial phase when the hypoxic cells would not be damaged

$$\overline{DEF_i} = \frac{fx_{tot}}{fx_{accel}} = 1 + \frac{\ln(M_i)}{\alpha_0 D_0}$$

$$\overline{DEF_i} < DEF_i$$

?

Radiotherapy and Oncology 180 (2023) 109491

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Visualization of tumor hypoxia and re-oxygenation after stereotactic body radiation therapy in early peripheral lung cancer: A prospective study

Masahiro Inada [a,*], Yasumasa Nishimura [a], Kohei Hanaoka [b], Kiyoshi Nakamatsu [a], Hiroshi Doi [a], Takuya Uehara [a], Mikihito Komanishi [b], Kazunari Ishii [c], Hayato Kaida [c], Makoto Hosono [a]

[a] *Departments of Radiation Oncology, Kindai University Faculty of Medicine;* [b] *Division of Positron Emission Tomography, Institute of Advanced Clinical Medicine, Kindai University; and* [c] *Departments of Radiology, Kindai University Faculty of Medicine, 377-2, Onohigashi, Osakasayama-city, Osaka, Japan*

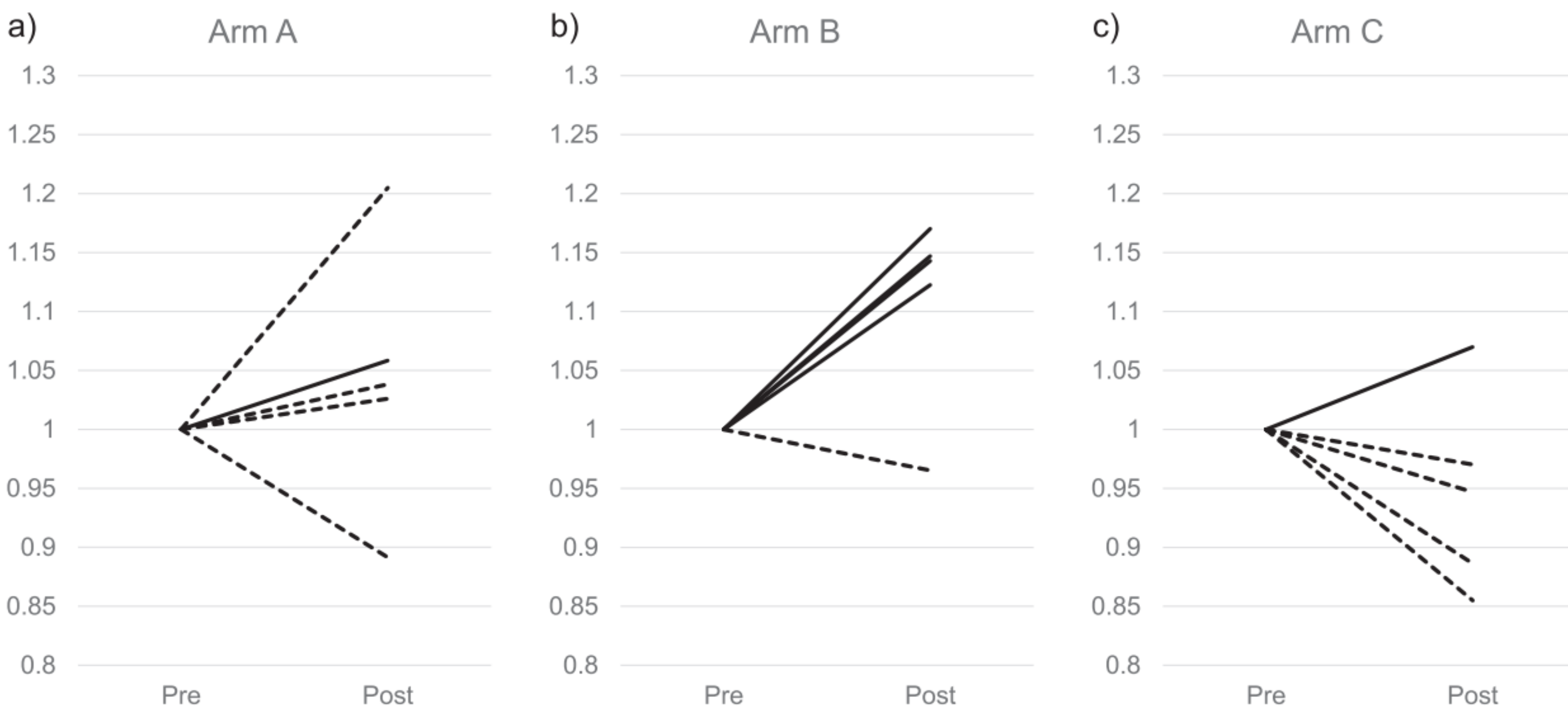
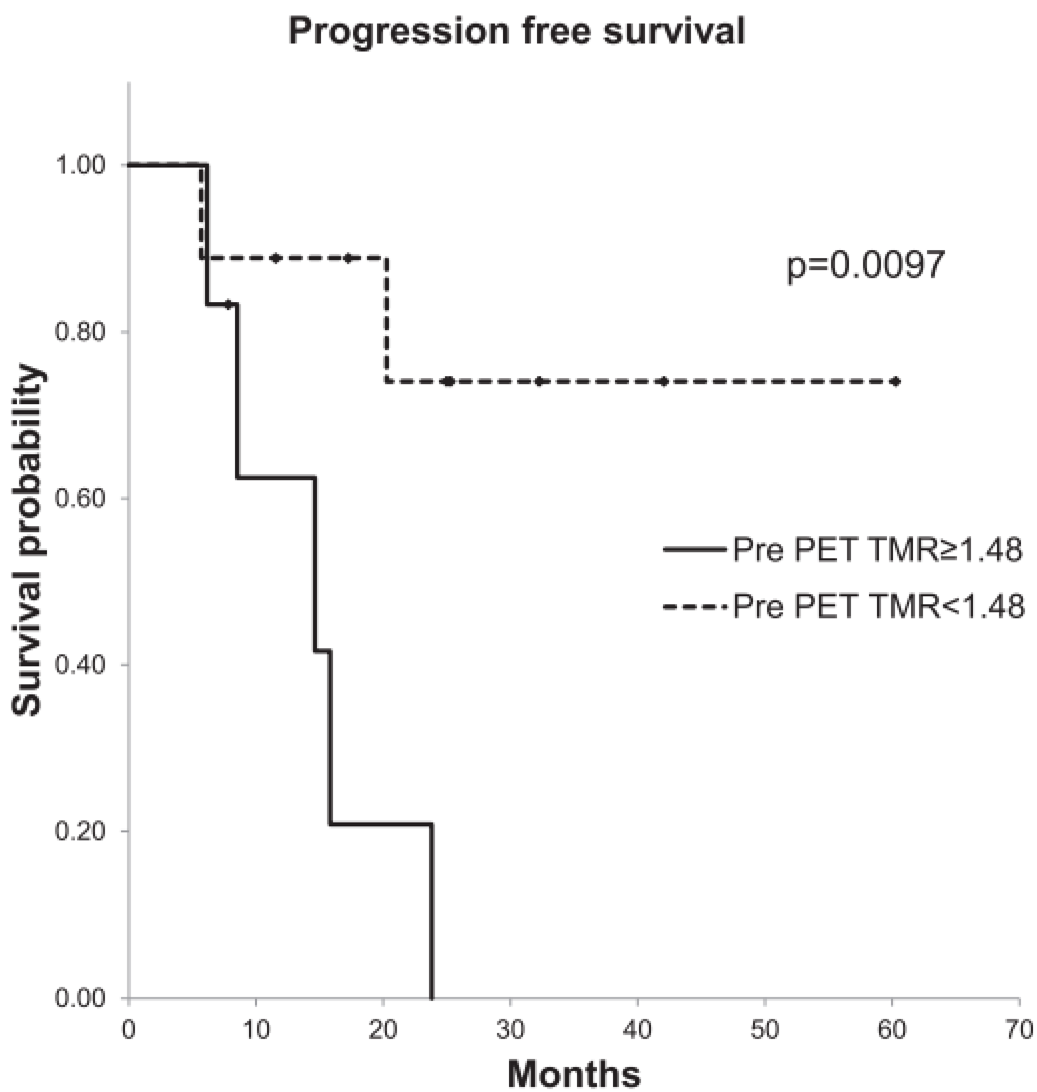


Fig. 3. The rate of change in TMR from pre-PET to post-PET in each tumor according to the treatment schedule arms. Pre-PET values were converted to 1.00 and post-PET values were converted into post-PET TMR divided by pre-PET TMR. a) in Arm A, b) in Arm B, c) in Arm C. Dotted lines indicate tumors with pre-treatment hypoxia, and solid lines tumors without pre-treatment hypoxia.

b)



Number at risk

TMR≥1.48	6	3	1	0	0	0	0
TMR<1.48	9	8	5	3	2	1	0

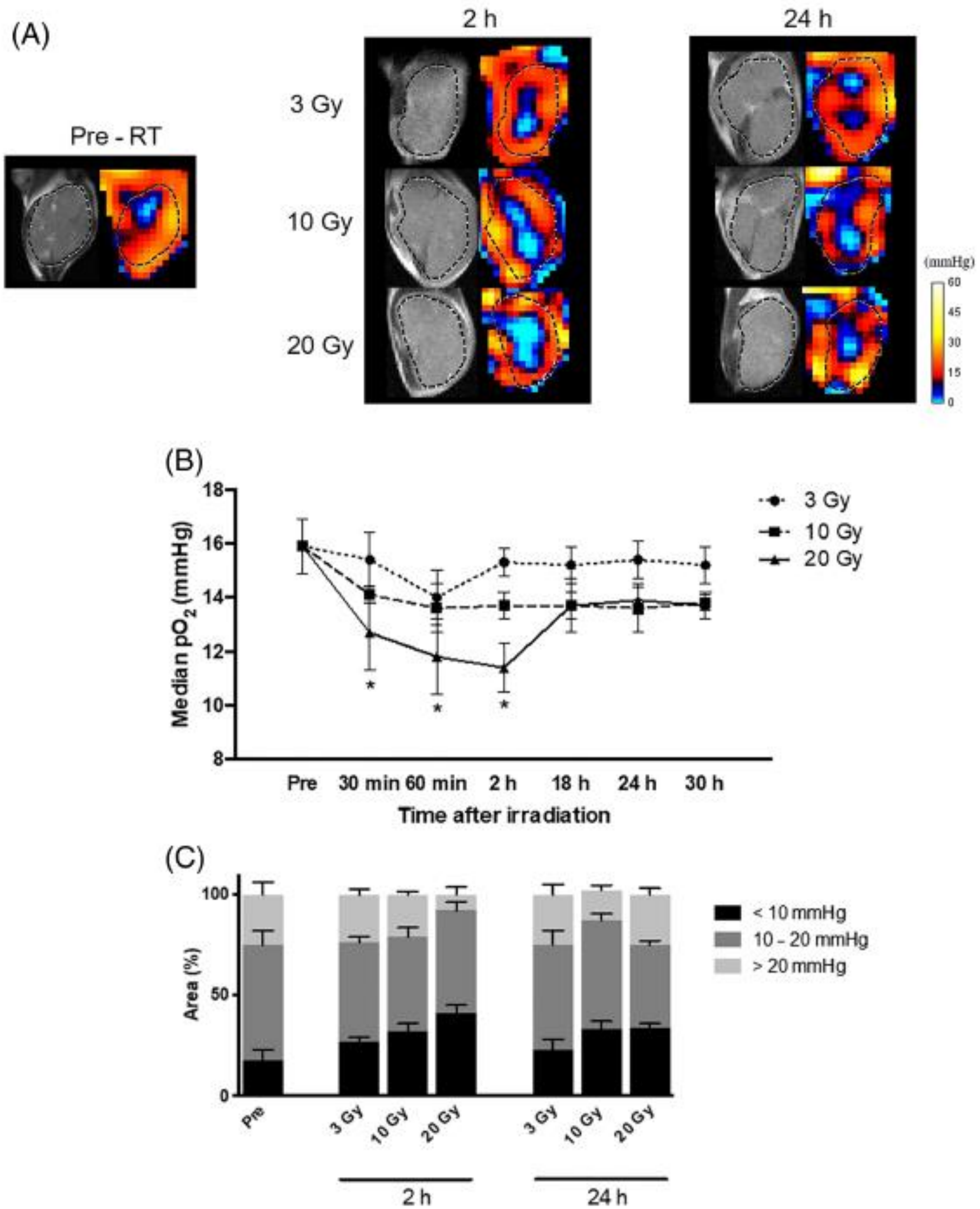
Received: 7 February 2022 | Revised: 17 May 2022 | Accepted: 1 June 2022
DOI: 10.1002/nbm.4783

RESEARCH ARTICLE

NMR IN BIOMEDICINE WILEY

Continuous monitoring of postirradiation reoxygenation and cycling hypoxia using electron paramagnetic resonance imaging

Tatsuya Kawai[1,2] | Masayuki Matsuo[3,4] | Yoichi Takakusagi[3,5] | Keita Saito[3] | Fuminori Hyodo[3,6] | Nallathamby Devasahayam[3] | Shingo Matsumoto[3,7] | Shun Kishimoto[3] | Hironobu Yasui[3,8] | Kazutoshi Yamamoto[3] | Murali C. Krishna[3]


(A)
Pre - RT
2 h
24 h
3 Gy
10 Gy
20 Gy
(mmHg)
60
45
30
15
0
(B)
Median pO2 (mmHg)
18
16
14
12
10
8
Pre
30 min
60 min
2 h
18 h
24 h
30 h
Time after irradiation
3 Gy
10 Gy
20 Gy
(C)
Area (%)
100
50
0
Pre
3 Gy
10 Gy
20 Gy
3 Gy
10 Gy
20 Gy
2 h
24 h
< 10 mmHg
10 - 20 mmHg
> 20 mmHg

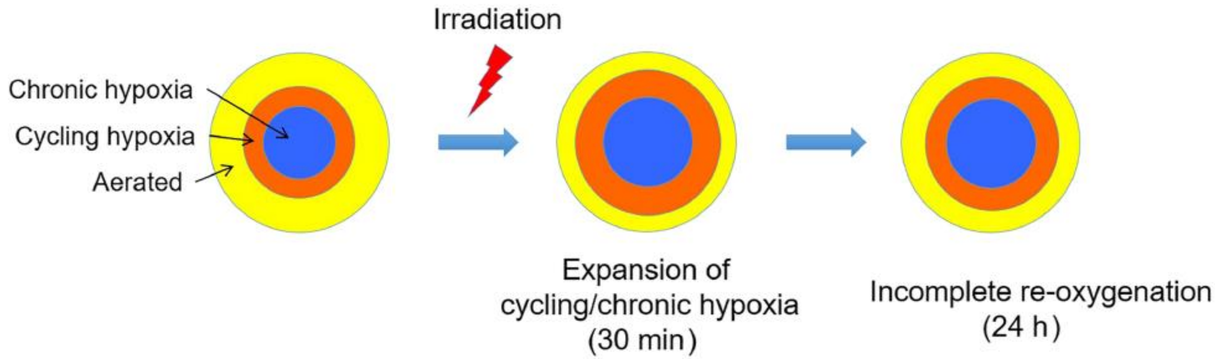


FIGURE 4 A schema of the biological effect of the radiation therapy against solid tumors considering cycling hypoxia in the reoxygenation process

Eur J Nucl Med Mol Imaging (2016) 43:2147–2154
DOI 10.1007/s00259-016-3431-4

ORIGINAL ARTICLE

The reoxygenation of hypoxia and the reduction of glucose metabolism in head and neck cancer by fractionated radiotherapy with intensity-modulated radiation therapy

Shozo Okamoto[1] · **Tohru Shiga**[1] · **Koichi Yasuda**[2] · **Shiro Watanabe**[1] · **Kenji Hirata**[1] · **Ken-ichi Nishijima**[3] · **Keiichi Magota**[1] · **Katsuhiko Kasai**[1] · **Rikiya Onimaru**[2] · **Kazuhiko Tuchiya**[2] · **Yuji Kuge**[3] · **Hiroki Shirato**[2] · **Nagara Tamaki**[1]

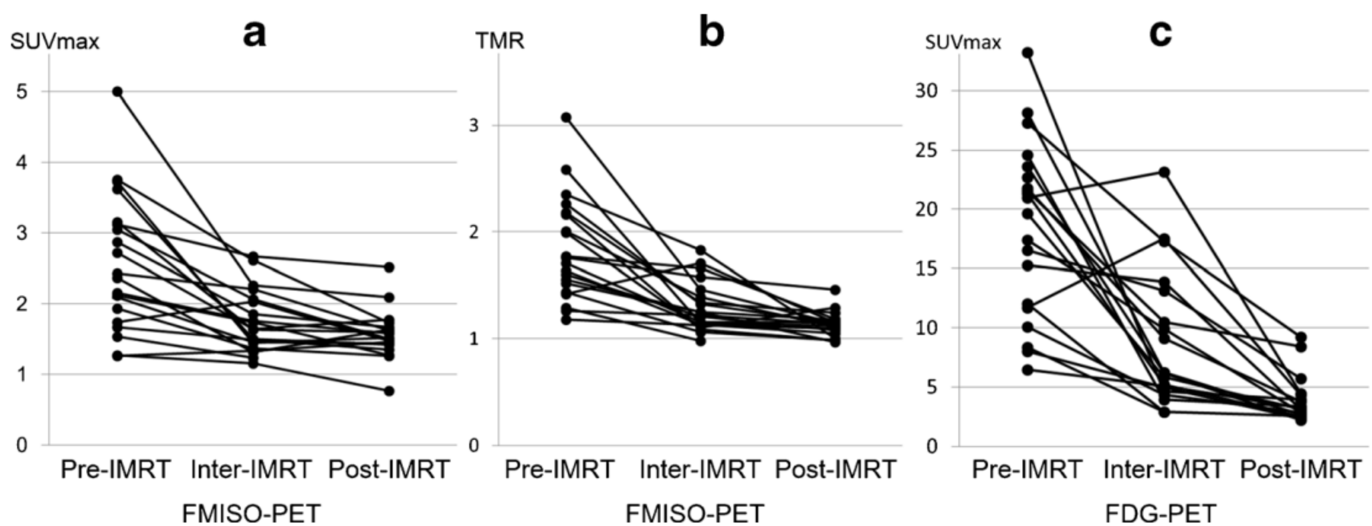


Fig. 2 Serial changes in the SUVmax analysis by FMISO-PET (**a**), the TMR analysis in FMISO-PET (**b**), and the SUVmax analysis in FDG-PET (**c**)

Radiotherapy and Oncology 105 (2012) 21–28

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

PET imaging of hypoxia

Exploratory prospective trial of hypoxia-specific PET imaging during radiochemotherapy in patients with locally advanced head-and-neck cancer

Daniel Zips [b,1], Klaus Zöphel [b,1], Nasreddin Abolmaali [b], Rosalind Perrin [a,*], Andrij Abramyuk [b], Robert Haase [a], Steffen Appold [b], Jörg Steinbach [c], Jörg Kotzerke [b,2], Michael Baumann [b,c,2]

[a] OncoRay National Center for Radiation Research in Oncology, Medical Faculty, Dresden University of Technology, Germany; [b] Medical Faculty and University Hospital Carl Gustav Carus, Dresden, Germany; [c] Helmholtz Research Center Dresden-Rossendorf, Germany

Published OnlineFirst January 11, 2016; DOI: 10.1158/1078-0432.CCR-15-1990

Cancer Therapy: Clinical

Clinical Cancer Research

Low Cancer Stem Cell Marker Expression and Low Hypoxia Identify Good Prognosis Subgroups in HPV(−) HNSCC after Postoperative Radiochemotherapy: A Multicenter Study of the DKTK-ROG

Annett Linge[1,2,3], Steffen Löck[3], Volker Gudziol[4], Alexander Nowak[5], Fabian Lohaus[1,2,3], Cläre von Neubeck[1,3], Martin Jütz[3], Amir Abdollahi[6,7,8,9,10], Jürgen Debus[6,7,8,9,11], Inge Tinhofer[12,13], Volker Budach[12,13], Ali Sak[14,15], Martin Stuschke[14,15], Panagiotis Balermpas[16,17], Claus Rödel[16,17], Melanie Avlar[18,19], Anca-Ligia Grosu[18,20], Christine Bayer[21], Claus Belka[21,22], Steffi Pigorsch[21,23], Stephanie E. Combs[21,23], Stefan Welz[24,25], Daniel Zips[24,25], Frank Buchholz[1,26], Daniela E. Aust[1,27,28], Gustavo B. Baretton[1,27,28], Howard D. Thames[29], Anna Dubrovska[1,3], Jan Alsner[30], Jens Overgaard[30], Michael Baumann[1,2,3,31,32], and Mechthild Krause[1,2,3,31,32] for the DKTK-ROG

Radiotherapy and Oncology 124 (2017) 533–540

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Prospective clinical trial

Residual tumour hypoxia in head-and-neck cancer patients undergoing primary radiochemotherapy, final results of a prospective trial on repeat FMISO-PET imaging

Steffen Löck [a,b,c,d,1], Rosalind Perrin [a,e,1], Annekatrin Seidlitz [a,c], Anna Bandurska-Luque [a,c], Sebastian Zschaeck [a,c,3], Klaus Zöphel [f,g], Mechthild Krause [a,c,d,g,h,i], Jörg Steinbach [g,j], Jörg Kotzerke [f,g], Daniel Zips [k,l], Esther G.C. Troost [a,c,d,g,h,*,2], Michael Baumann [a,c,d,g,h,i,2]

[a] OncoRay – National Center for Radiation Research in Oncology, Biostatistics and Modeling in Radiation Oncology Group; [b] OncoRay – National Center for Radiation Research in Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Helmholtz-Zentrum Dresden-Rossendorf; [c] Department of Radiotherapy and Radiation Oncology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden; [d] German Cancer Consortium (DKTK), partner site Dresden, Germany; [e] Center for Proton Therapy, Paul Scherrer Institute, Switzerland; [f] Department of Nuclear Medicine, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden; [g] National Center for Tumor Diseases, partner site Dresden; [h] Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiooncology – OncoRay; [i] Deutsches Krebsforschungszentrum (DKFZ), Heidelberg; [j] Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiopharmaceutical Cancer Research; [k] Department of Radiation Oncology, Eberhard Karls Universität Tübingen; and [l] German Cancer Consortium (DKTK), partner site Tübingen, Germany

Michael Bauman

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: http://www.tandfonline.com/loi/ionc20

Robustness of quantitative hypoxia PET image analysis for predicting local tumor control

David Mönnich, Stefan Welz, Daniela Thorwarth, Christina Pfannenberg, Gerald Reischl, Paul-Stefan Mauz, Konstantin Nikolaou, Christian la Fougère & Daniel Zips

Acta Oncologica

ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: http://www.tandfonline.com/loi/ionc20

Spatial distribution of FMISO in head and neck squamous cell carcinomas during radio-chemotherapy and its correlation to pattern of failure

Sebastian Zschaeck, Robert Haase, Nasreddin Abolmaali, Rosalind Perrin, Kristin Stützer, Steffen Appold, Jörg Steinbach, Jörg Kotzerke, Daniel Zips, Christian Richter, Volker Gudziol, Mechthild Krause, Klaus Zöphel & Michael Baumann

S. Löck et al. / Radiotherapy and Oncology 124 (2017) 533–540

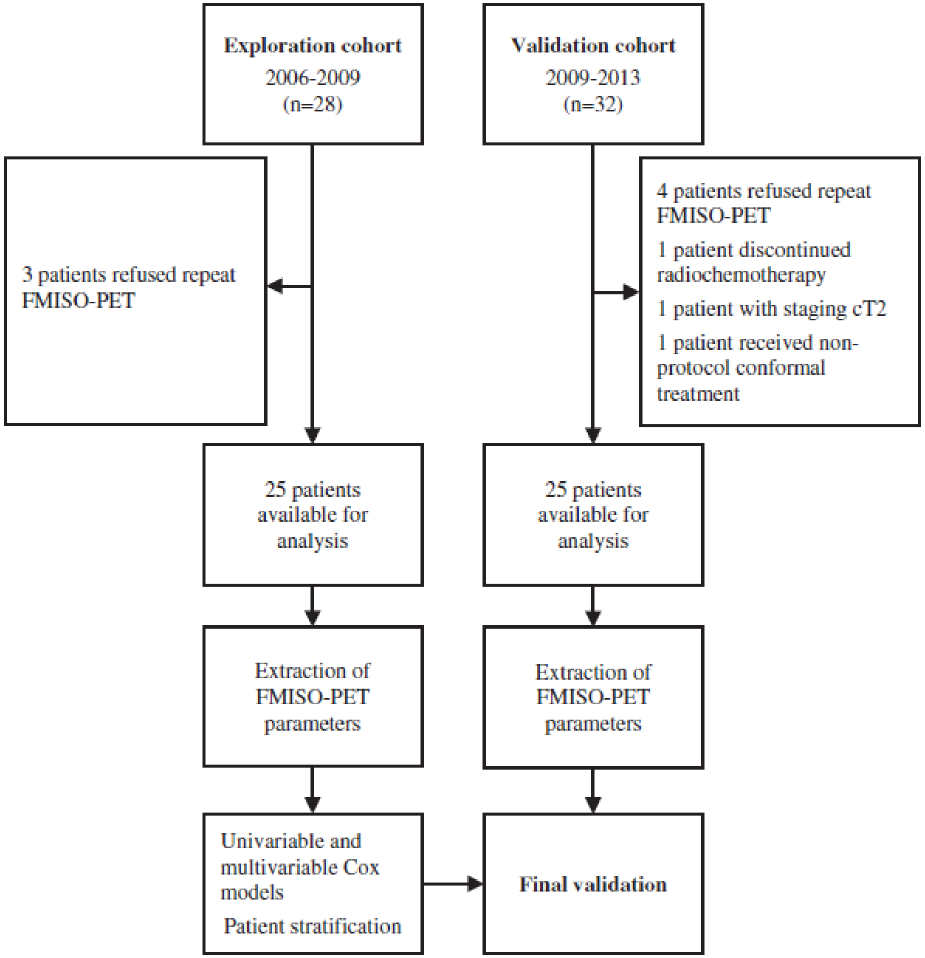
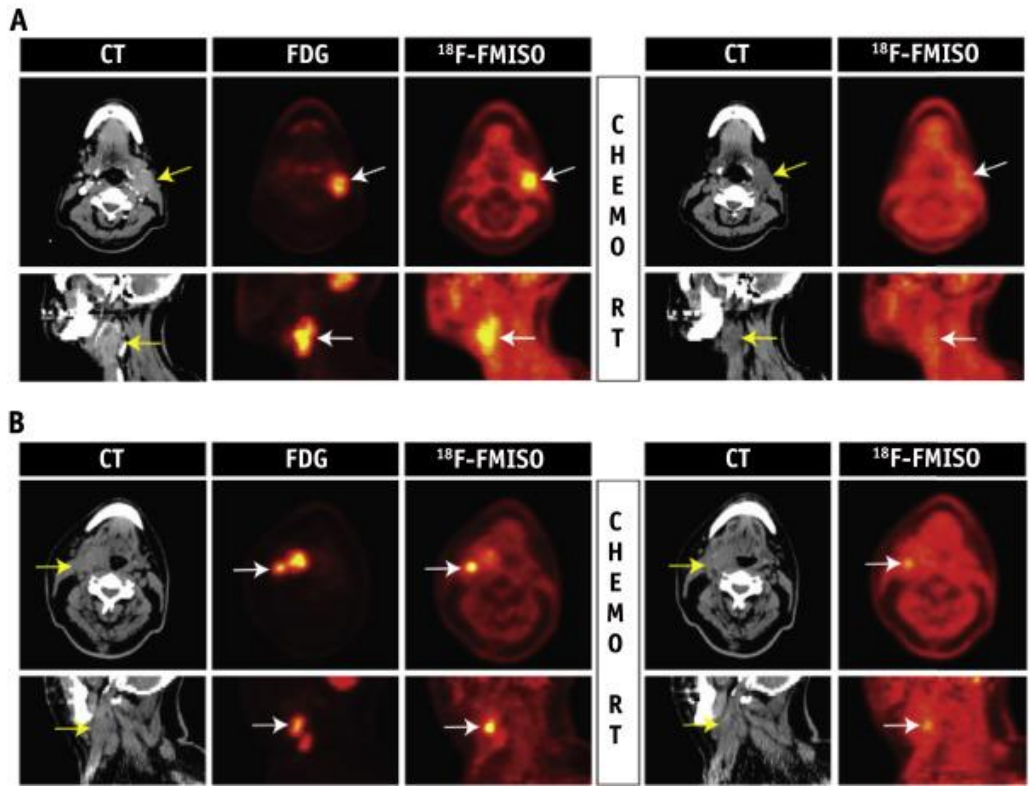


Fig. 1. Study design.

Lack of re-oxygenation at 2 weeks is the key



MedAustron

Loco regional control of HPV- locally advanced OPC

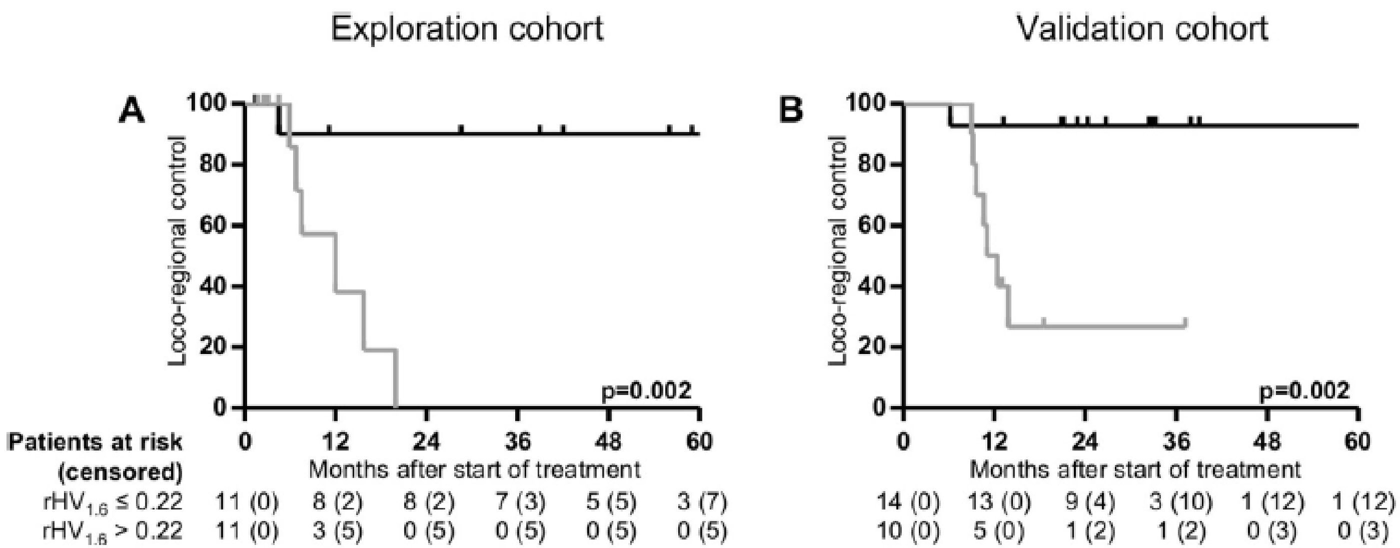


Fig. 2. Patient stratification by residual tumour hypoxia after second week of treatment: loco-regional tumour control of patients in the exploration cohort (A) and the validation cohort (B), stratified by the median individual residual tumour hypoxia determined after the second week of treatment in the exploration cohort. Residual tumour hypoxia was defined as ratio of $HV_{1.6}$ after the second week of treatment and the corresponding pre-treatment HV.

Carbon and hypoxia

Present

- We know what hypoxia does to carbon

Future

- We want to know what carbon does to hypoxia

Hypoxia and reoxygenation

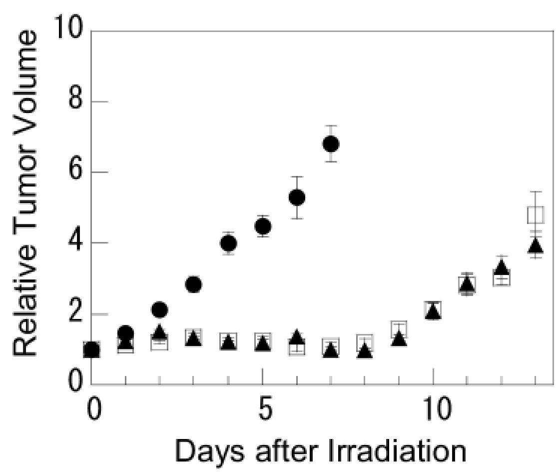


Fig. 1. Volume changes of the NFSa fibrosarcomas after irradiation. Closed circles, closed triangles, and open squares are untreated, X-ray, and carbon-ion irradiated tumors, respectively. The symbols and bars are the mean and SEM calculated from five mice each.

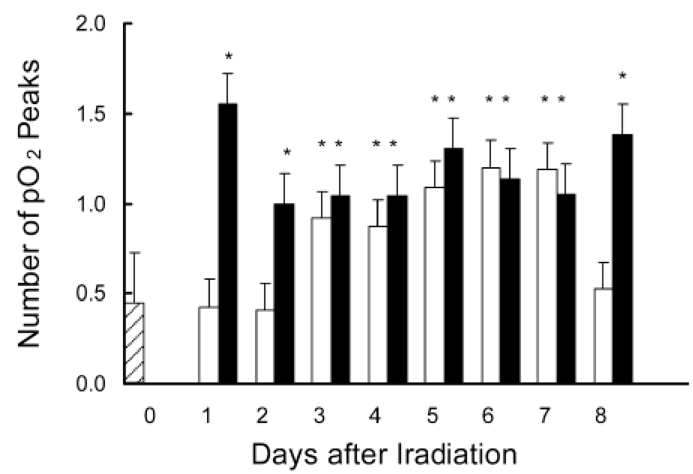


Fig. 3. Time course of the number of pO_2 peaks after irradiation. The average number of pO_2 peaks was calculated from 20–25 pO_2 profiles per day for each group. The striped, white, and black bars are untreated, X-ray, or carbon-ion irradiated tumors, respectively. The error bars indicate SEM. The statistical significance ($*p < 0.05$) was obtained between untreated and irradiated tumors.

Fukawa et al. 2004

Int. J. Radiat. Biol., Vol. 82, No. 10, October 2006, pp. 699–757

Hypoxia: Importance in tumor biology, noninvasive measurement by imaging, and value of its measurement in the management of cancer therapy

Chairs
James L. Tatum, *Cancer Imaging Program, Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI)*
Gary J. Kelloff, *Cancer Imaging Program, Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI)*
Robert J. Gillies, *Arizona Cancer Center*

Reality is a complex thing

’Hypoxia promotes adaptive processes that lead to tumor aggressiveness, progression, and acquired resistance to treatment … Changes dependent on hypoxia inducible factors
(HIF) trigger metabolic adaptation, improved systemic oxygen supply, cell survival, and cell proliferation. Changes independent of HIF promote resistance to apoptosis and suppression of anticancer immune response. Tumors with pO2 values less than 1 mm Hg exhibit genomic changes such as point mutations, chromosomal aberrations, gene amplification, and polyploidy. Genetic instability results in the emergence of new genetic variants that can survive under otherwise lethal conditions, leading to a Darwinian selection process of the most resistant clones’

Published in final edited form as:
Immunohorizons. ; 3(4): 149–160. doi:10.4049/immunohorizons.1900017.

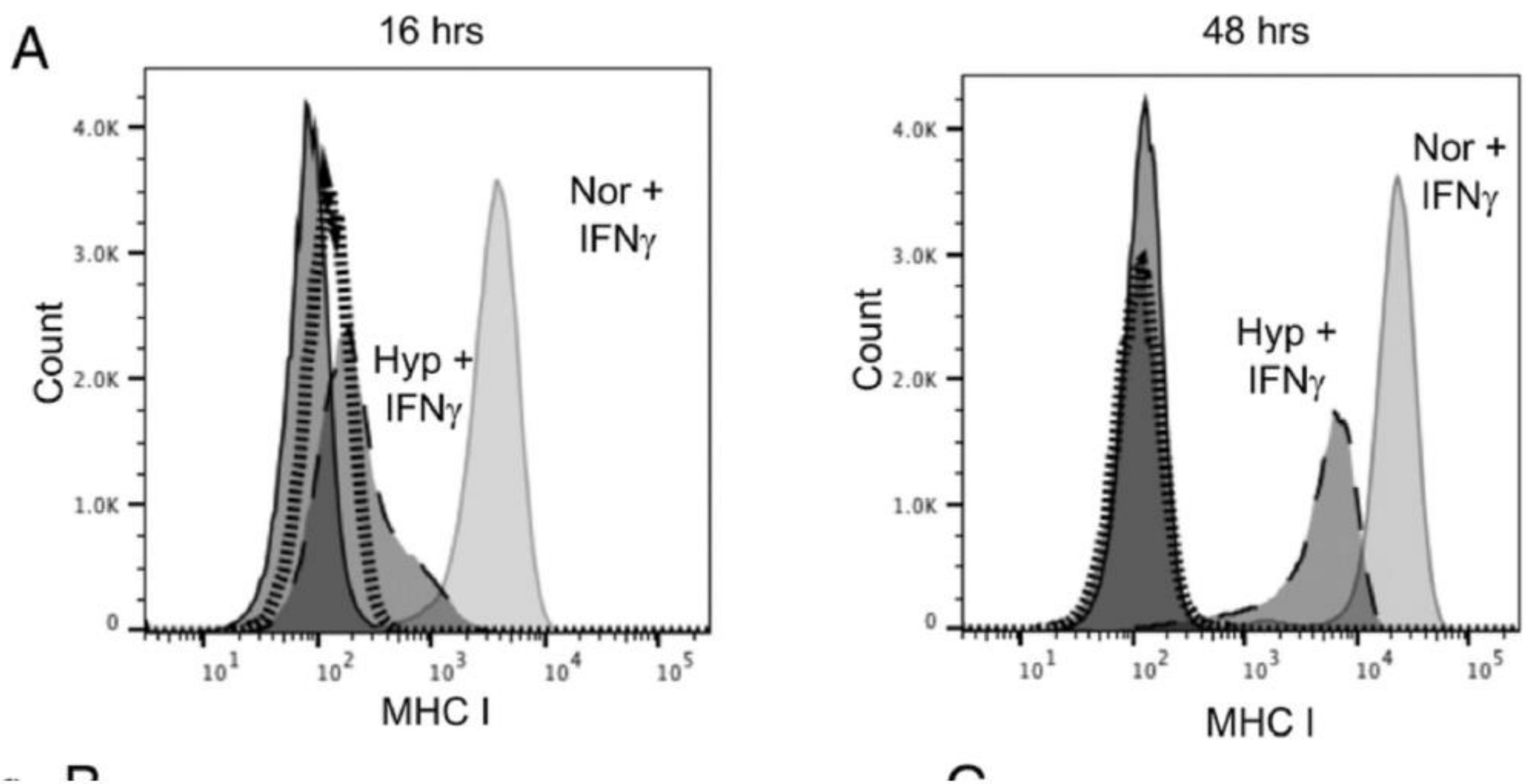
Intratumoral Hypoxia Reduces IFN-γ–Mediated Immunity and MHC Class I Induction in a Preclinical Tumor Model

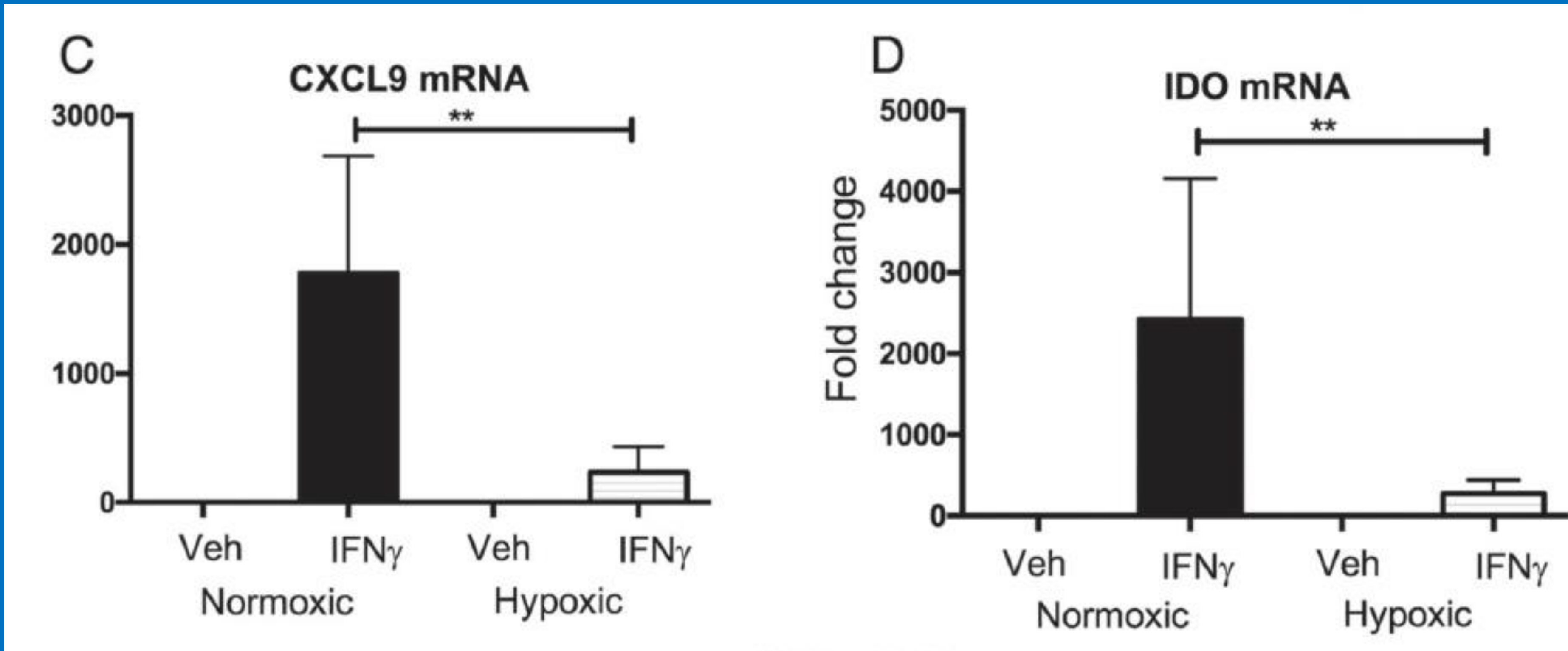
Aditi Murthy[*], **Scott A. Gerber**[*,†], **Cameron J. Koch**[‡], **Edith M. Lord**[*]

[*]Department of Microbiology and Immunology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642

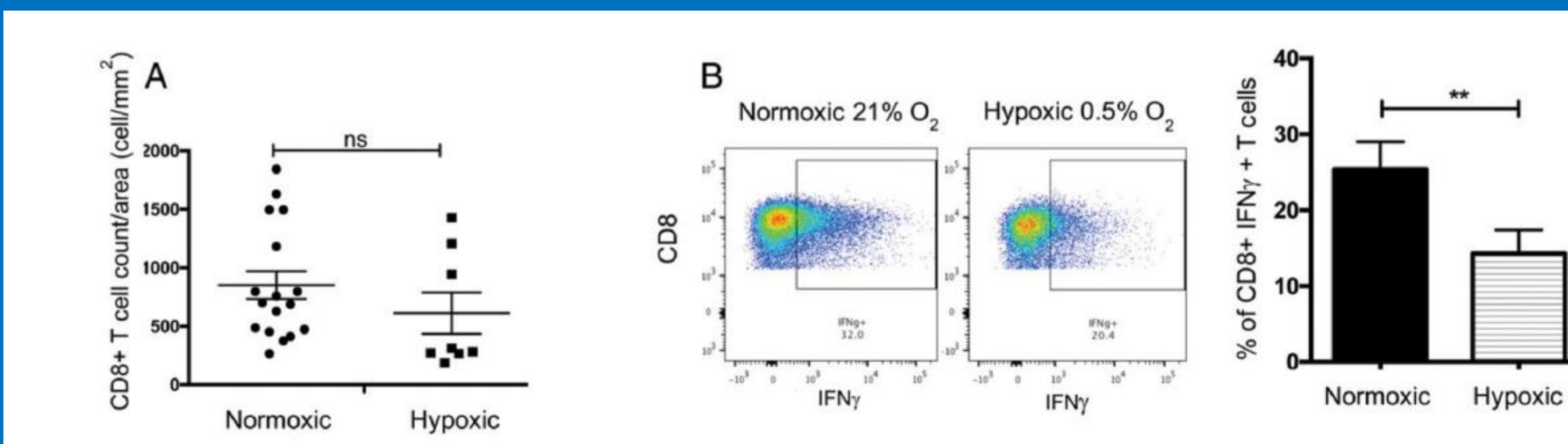
[†]Department of Surgery, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642

[‡]Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA 19104


A
16 hrs
48 hrs
Count
4.0K
3.0K
2.0K
1.0K
0
Nor +
IFNγ
Hyp +
IFNγ
MHC I



C
CXCL9 mRNA
3000
2000
1000
0
**
Veh
IFNγ
Veh
IFNγ
Normoxic
Hypoxic
D
IDO mRNA
Fold change
5000
4000
3000
2000
1000
0
**
Veh
IFNγ
Veh
IFNγ
Normoxic
Hypoxic



A
CD8+ T cell count/area (cell/mm2)
2000
1500
1000
500
0
ns
Normoxic
Hypoxic
B
Normoxic 21% O2
Hypoxic 0.5% O2
CD8
IFNγ
IFNγ
IFNg+
32.0
IFNg+
20.4
% of CD8+ IFNγ + T cells
40
30
20
10
0
**
Normoxic
Hypoxic

Vielen Dank für ihre Aufmerksamkeit

Vacancies

Karl Landsteiner University of Health Sciences/MedAustron

POSTDOCTORAL RESEARCH FELLOW (POST DOC) DIVISION „RADIATION ONCOLOGY" - UNIV. PROF. DR. PIERO FOSSATI MD
40 Hours (F/M/D)

PHD Position - DIVISION „RADIATION ONCOLOGY" - UNIV. PROF. DR. PIERO FOSSATI MD
30 Hours (F/M/D)

PHD Position - DIVISION „MEDICAL PHYSICS" - UNIV.-PROF. PD DI MARKUS STOCK, PHD
30 Hours (F/M/D)

Workplace: MedAustron in Wiener Neustadt

For more details contact:

martina.mascha@medaustron.at