9/30/2005

Imaging for Cancer Therapy

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DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

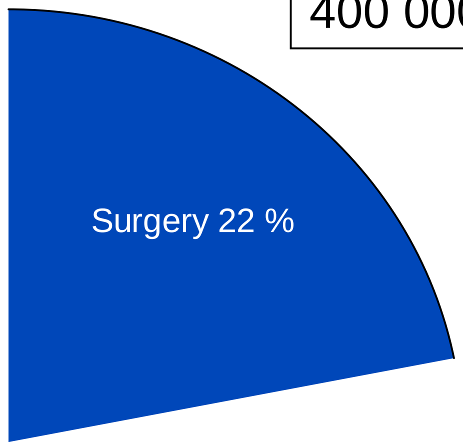
State of the art in Cancer Therapy

Cancer incidence
in Germany
400 000 / y

State of the art in Cancer Therapy

Cancer can be cured by:

Cancer incidence in Germany 400 000 / y



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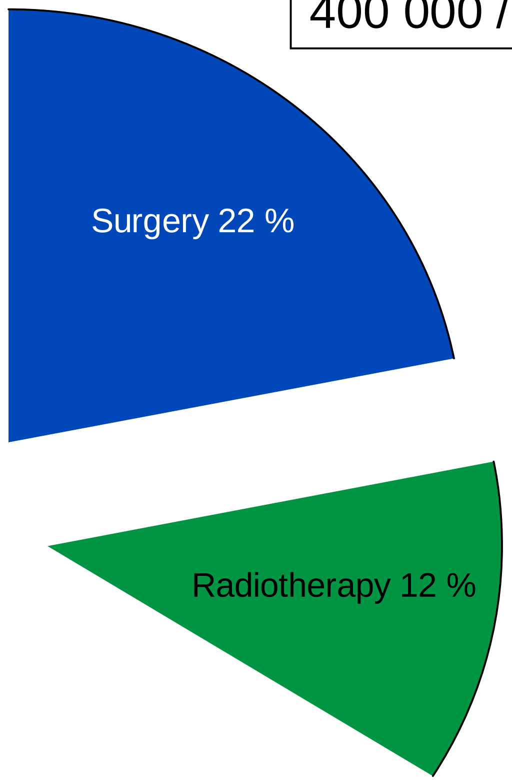

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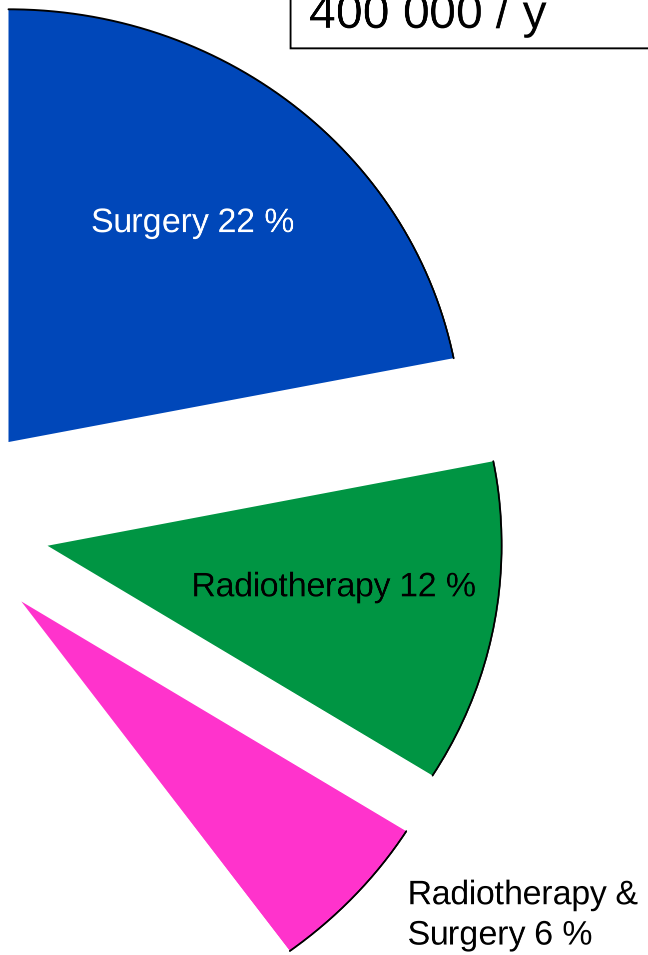

State of the art in Cancer Therapy

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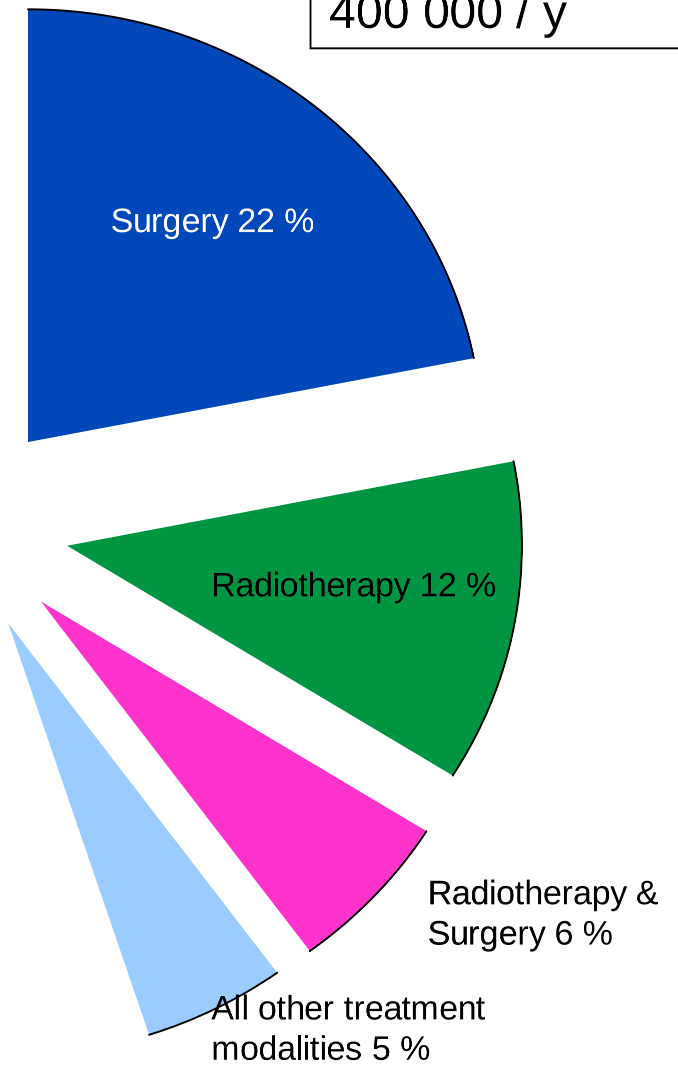

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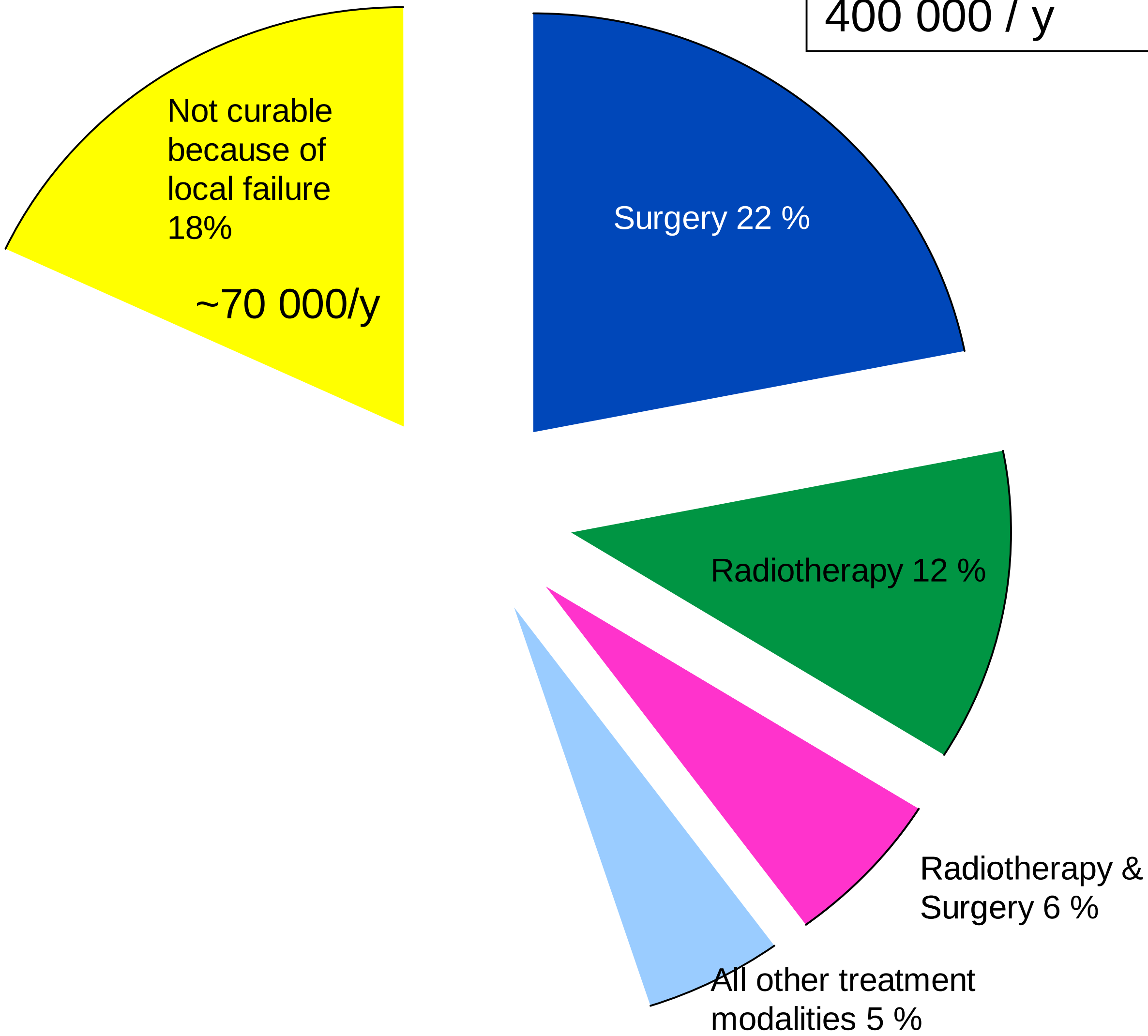

State of the art in Cancer Therapy

Cancer incidence in Germany 400 000 / y

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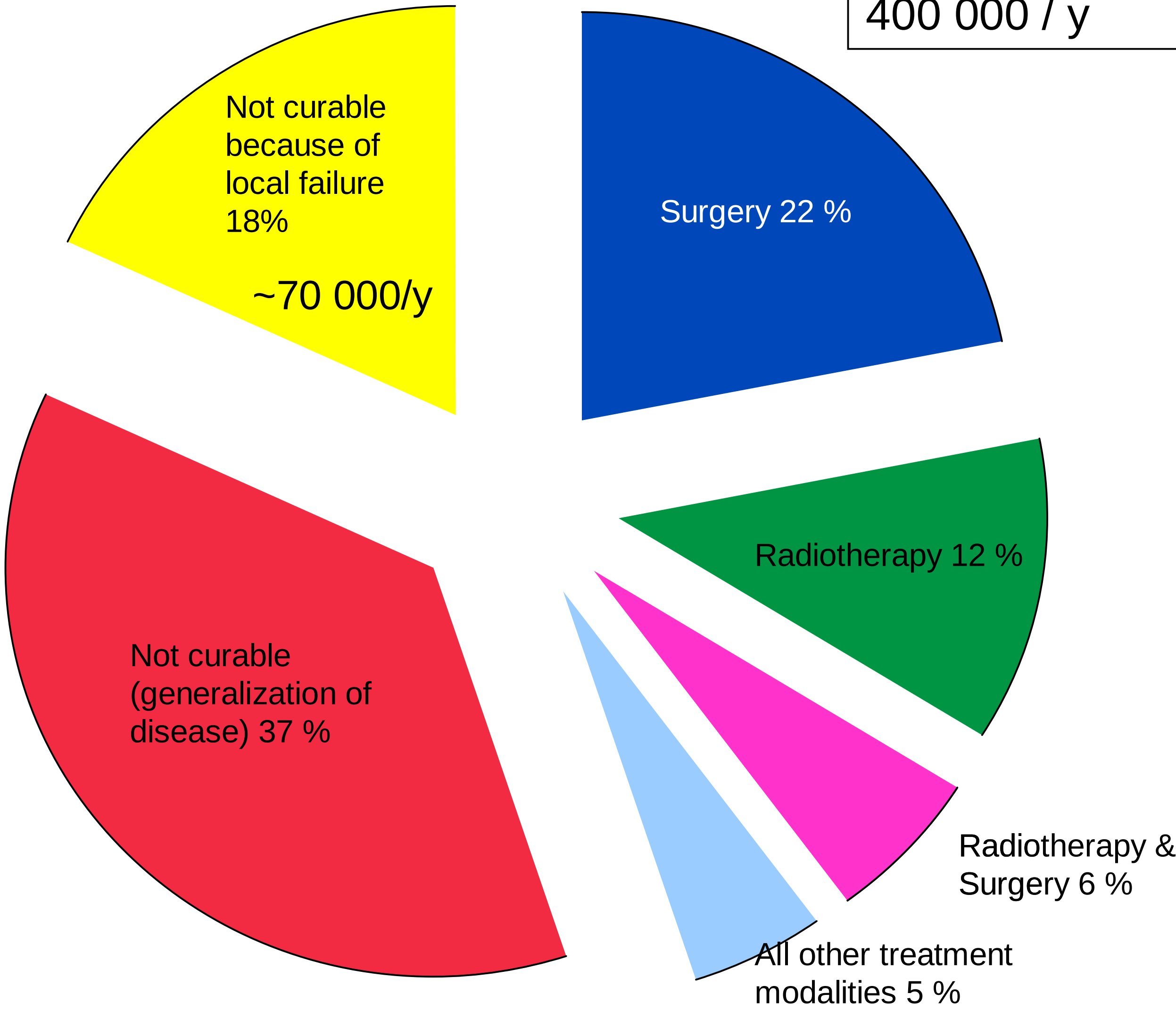
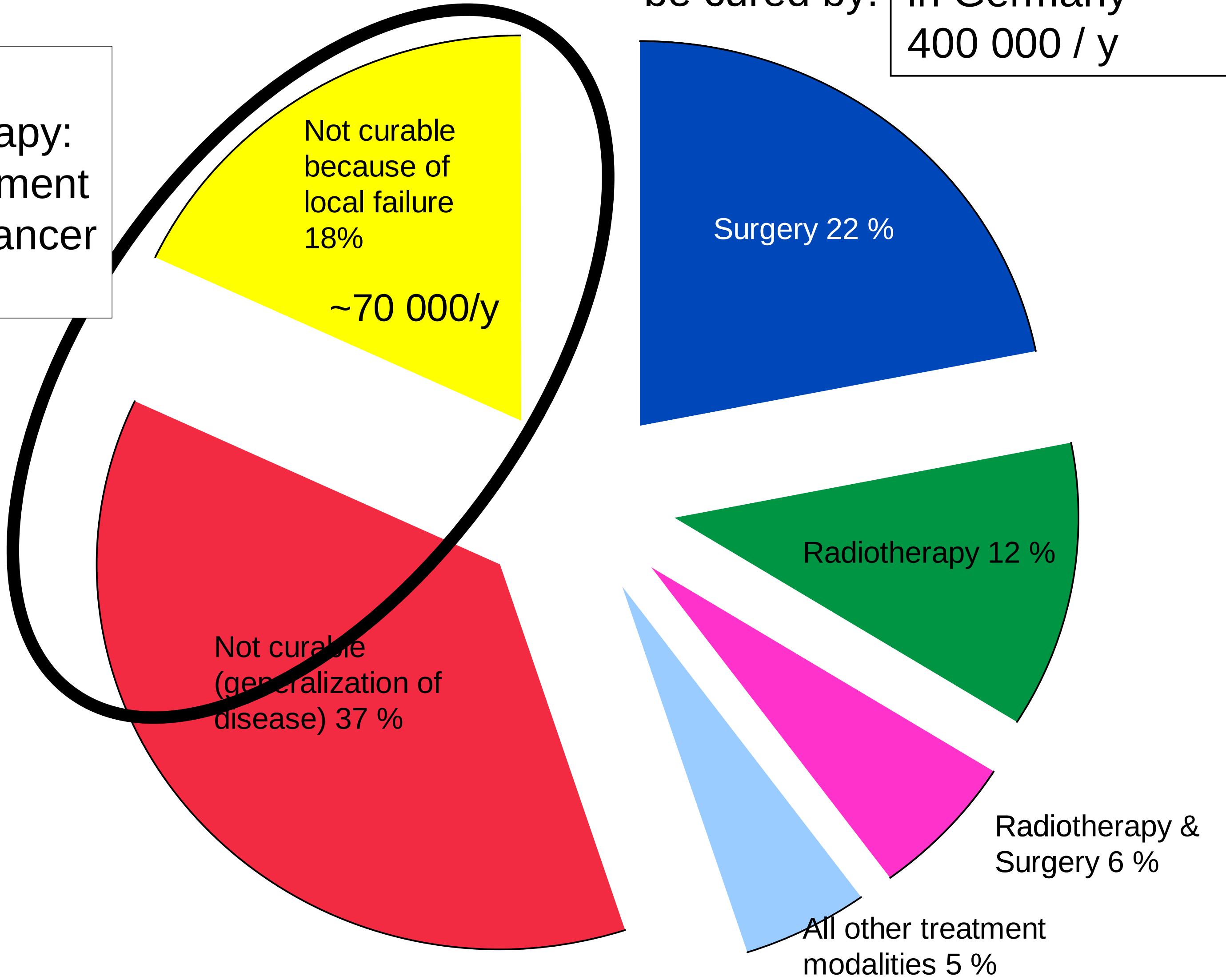


State of the art in Cancer Therapy

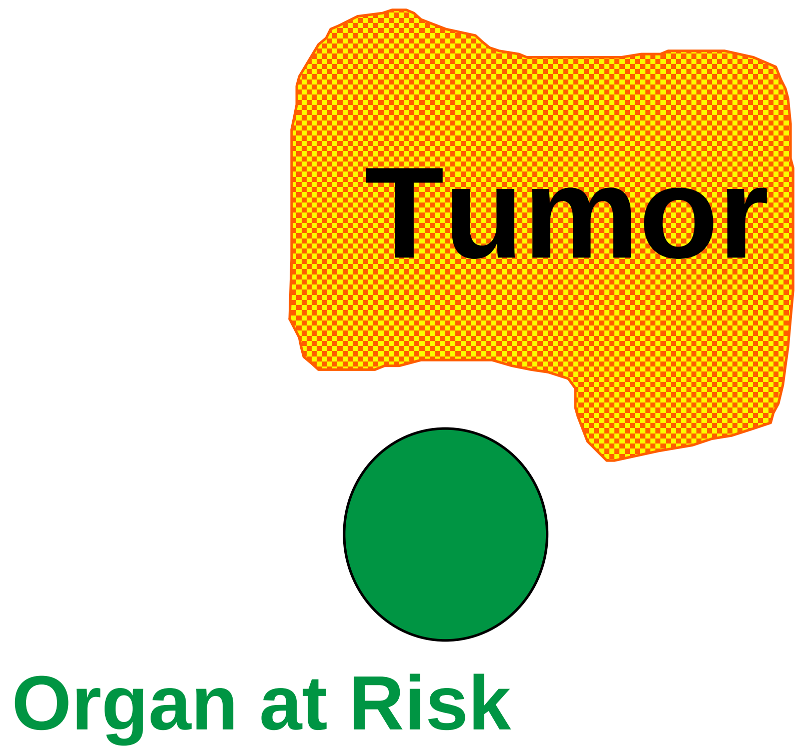
Cancer can be cured by:

Cancer incidence in Germany 400 000 / y

The goal of radiation therapy: Improve treatment of localized cancer



The targeting problem in Radiotherapy



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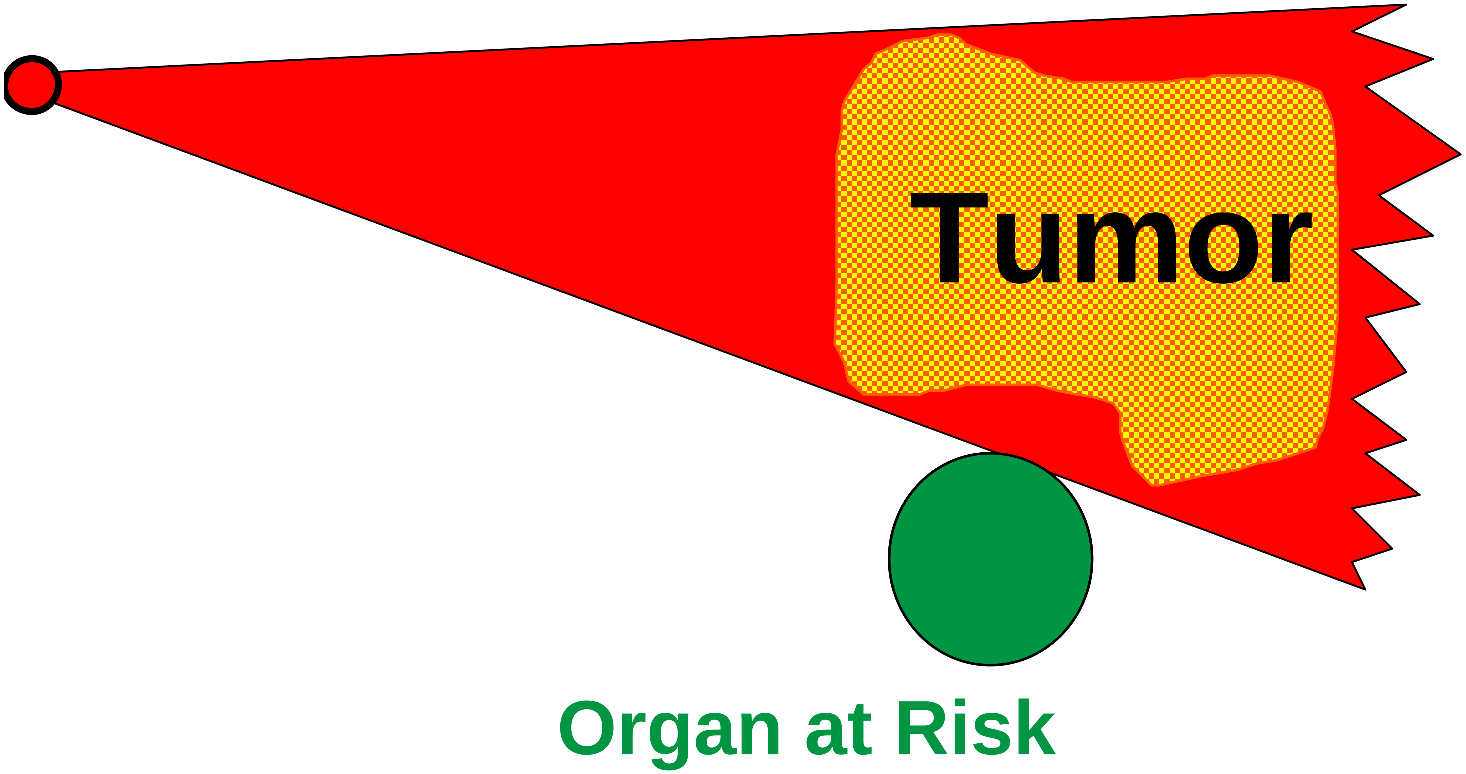

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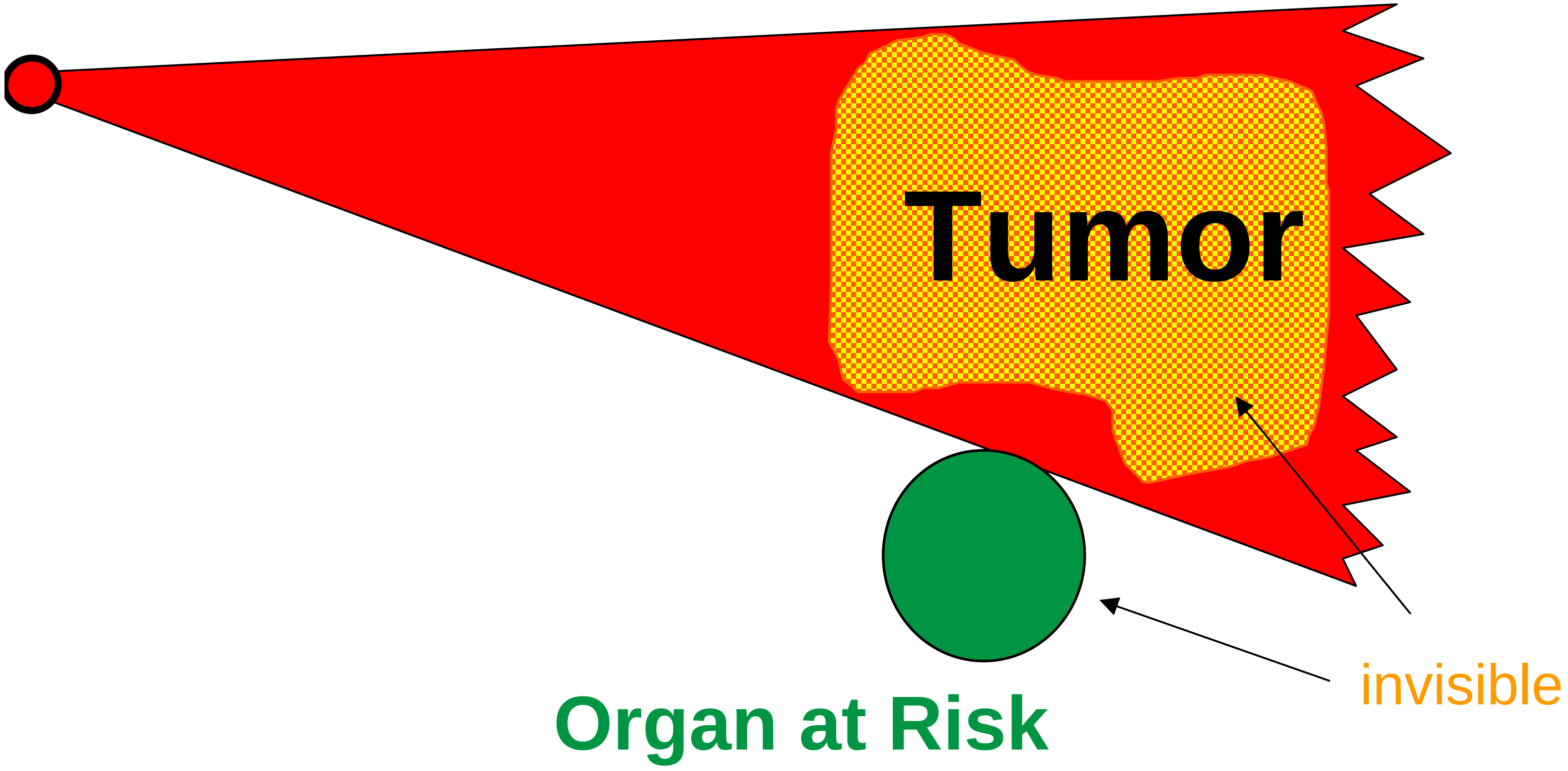

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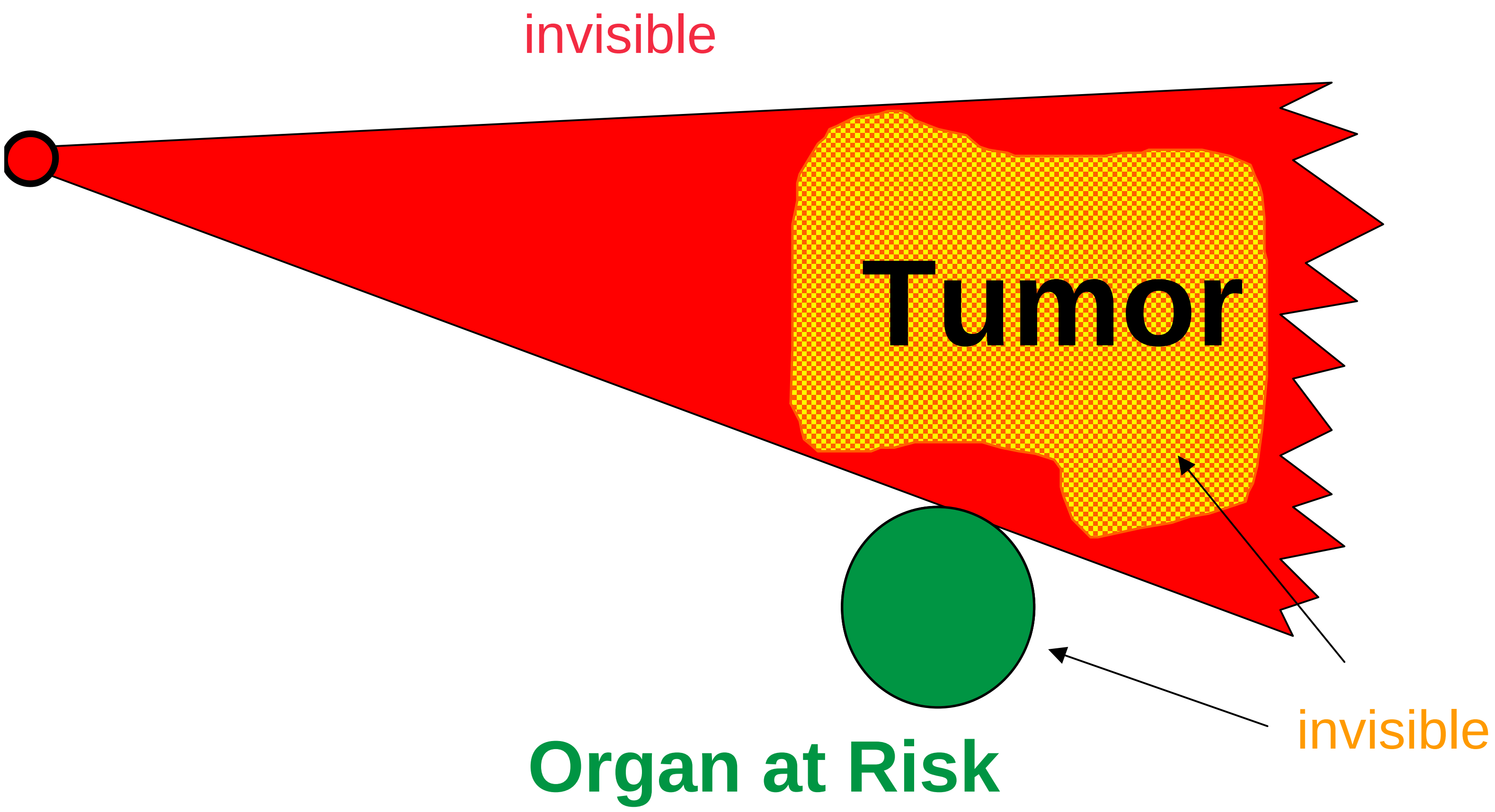


Radiotherapy is the art of hitting an invisible target with invisible irradiation

Radiotherapy is the art of hitting an invisible target with invisible irradiation

⬇

Targeting Problem

Radiotherapy is the art of hitting an invisible target with invisible irradiation

Targeting Problem

Tumor

Radiotherapy is the art of hitting an invisible target with invisible irradiation

↓

Targeting Problem

↓

Tumor

Organs at risk/
Normal tissue

Radiotherapy is the art of hitting an invisible target with invisible irradiation

Targeting Problem

Dose as high as possible

Tumor

Organs at risk/ Normal tissue

Radiotherapy is the art of hitting an invisible target with invisible irradiation

↓

Targeting Problem

↓

Dose as high as possible	**Tumor**
Dose as low as possible	**Organs at risk/ Normal tissue**

Radiotherapy is the art of hitting an invisible target with invisible irradiation

↓

Targeting Problem

↓

Dose as high as possible	**Tumor**	}
Dose as low as possible	**Organs at risk/ Normal tissue**	

Radiotherapy is the art of hitting an invisible target with invisible irradiation

↓

Targeting Problem

↓

Dose as high as possible	**Tumor**	}	**1. Space (Morphology)**
Dose as low as possible	**Organs at risk/ Normal tissue**		

Radiotherapy is the art of hitting an invisible target with invisible irradiation

Targeting Problem

Dose as high as possible	**Tumor**		**1. Space (Morphology)**
Dose as low as possible	**Organs at risk/ Normal tissue**		**2. Time (Movement)**

Radiotherapy is the art of hitting an invisible target with invisible irradiation

↓

Targeting Problem

↓

Dose as high as possible	**Tumor**	}	**1. Space (Morphology)**
Dose as low as possible	**Organs at risk/ Normal tissue**		**2. Time (Movement)**
			3. Biology (Molecular Profiling)

The 3 tasks in

Morphology

Where is primary tumour tissue ?

Where are affected lymph nodes and metastases ?

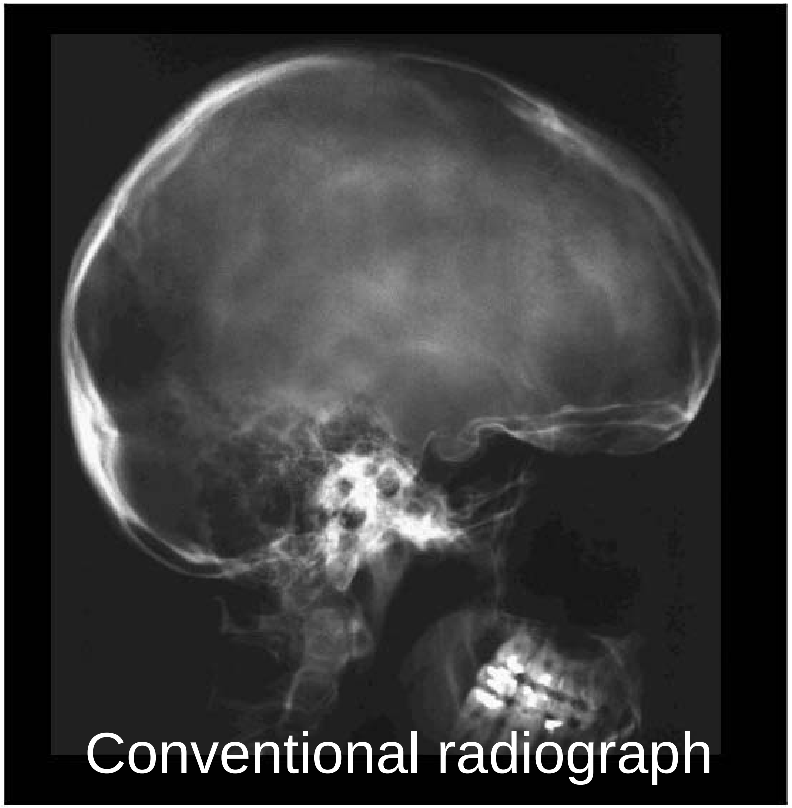
Where is radiosensitive normal tissue ?

Morphology

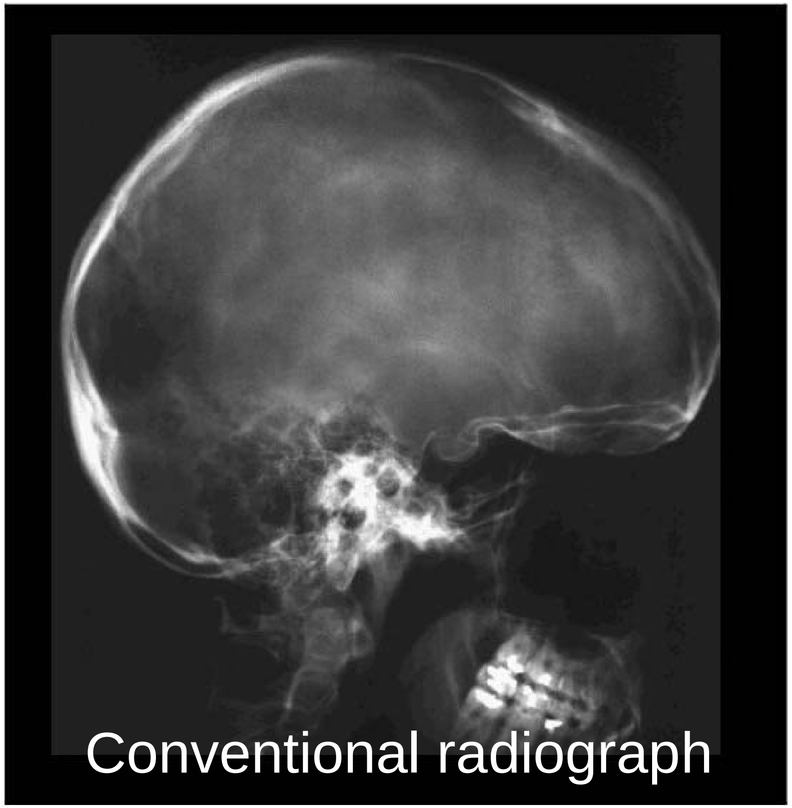
1. Detect the primary tumour
(including all tumour extensions) !

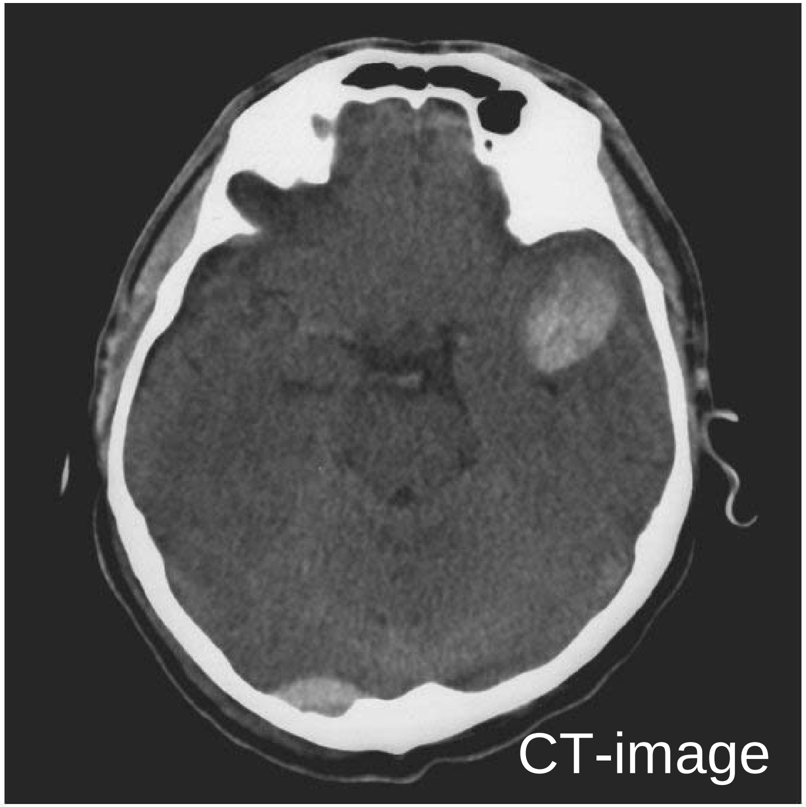
Morphology

Morphology

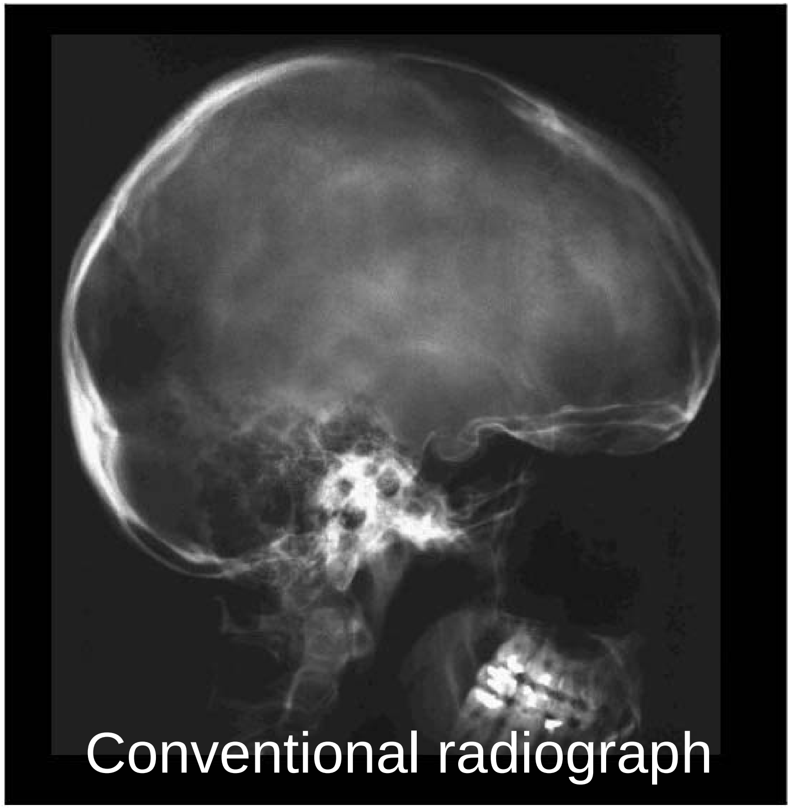

Conventional radiograph

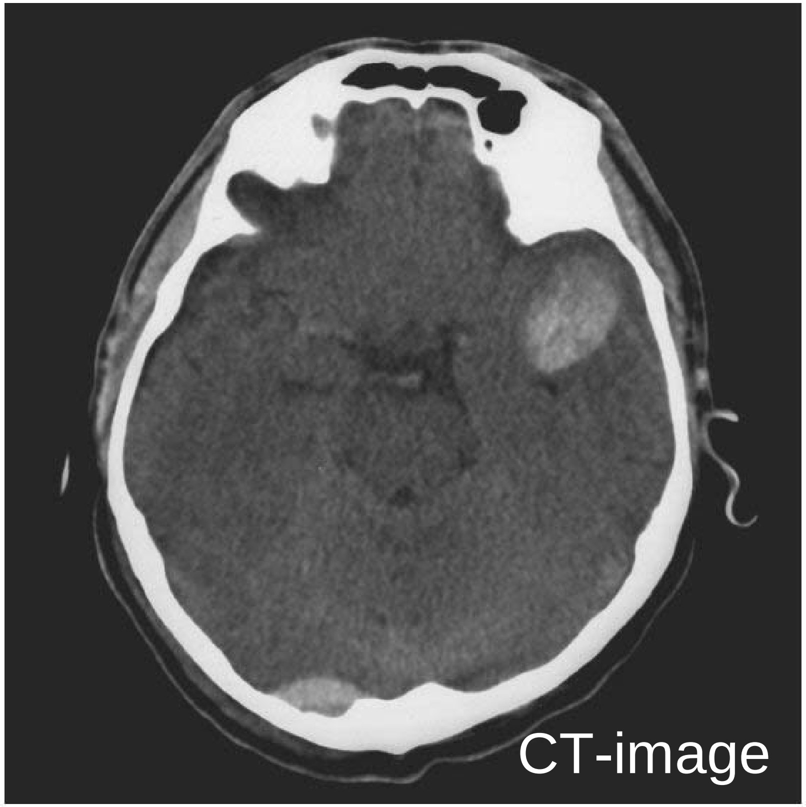
Morphology





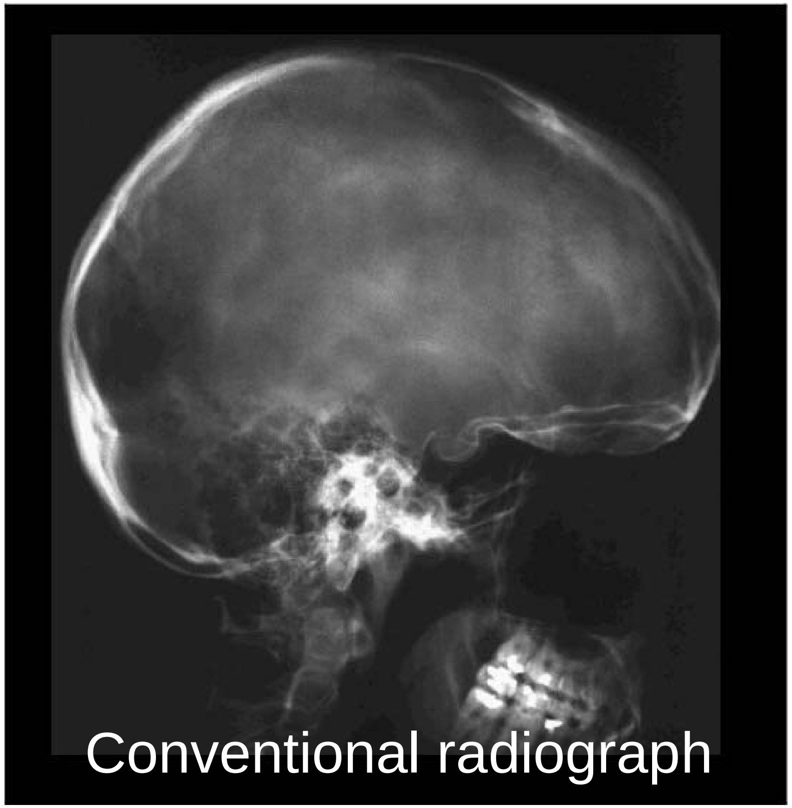
Morphology

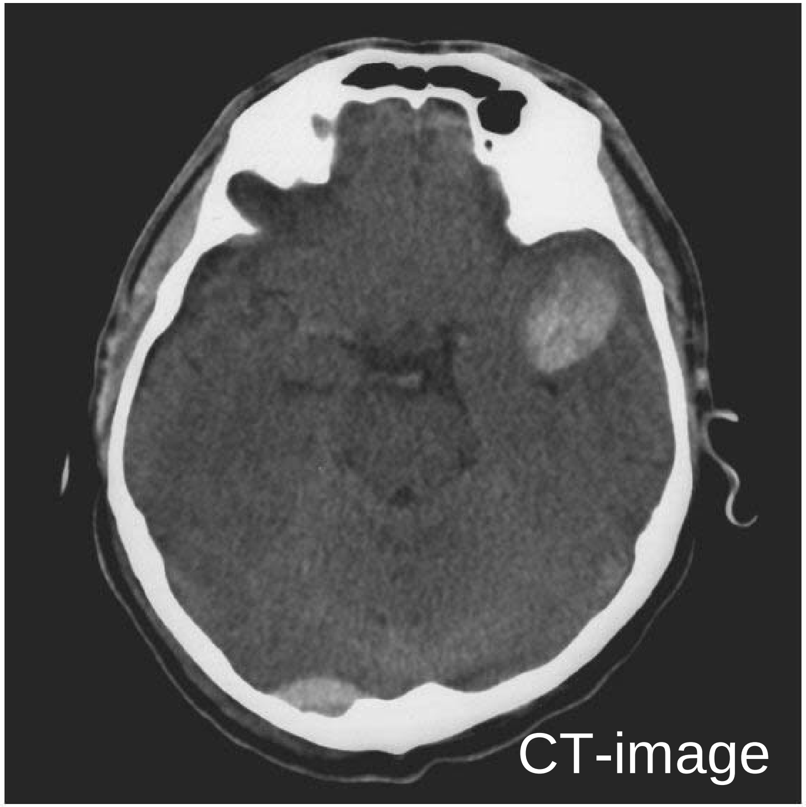




The 1st revolution in imaging for Radiation Oncology:
from 2D (Radiography with X-rays)
to 3D (Computerized Tomogrpahy, CT)!!

Morphology

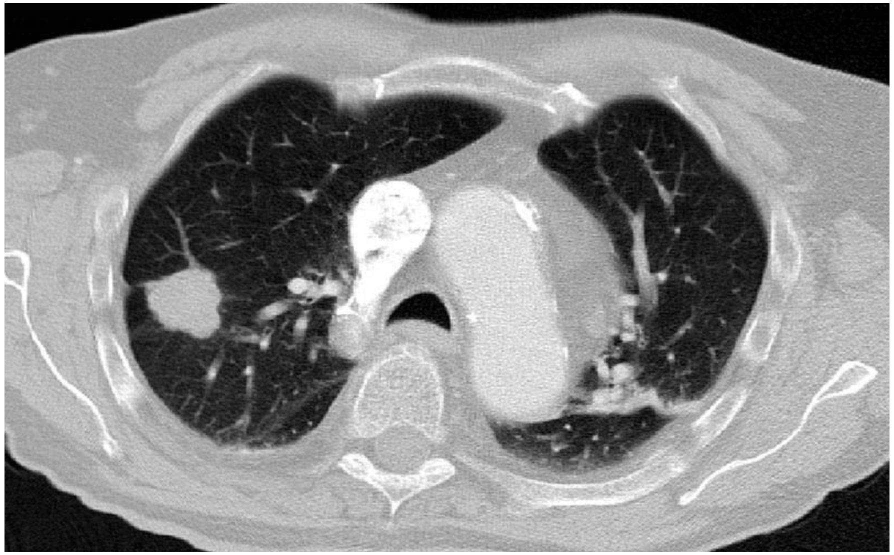




The 1st revolution in imaging for Radiation Oncology:
from 2D (Radiography with X-rays)
to 3D (Computerized Tomogrpahy, CT)!! ➔ 1980-1990

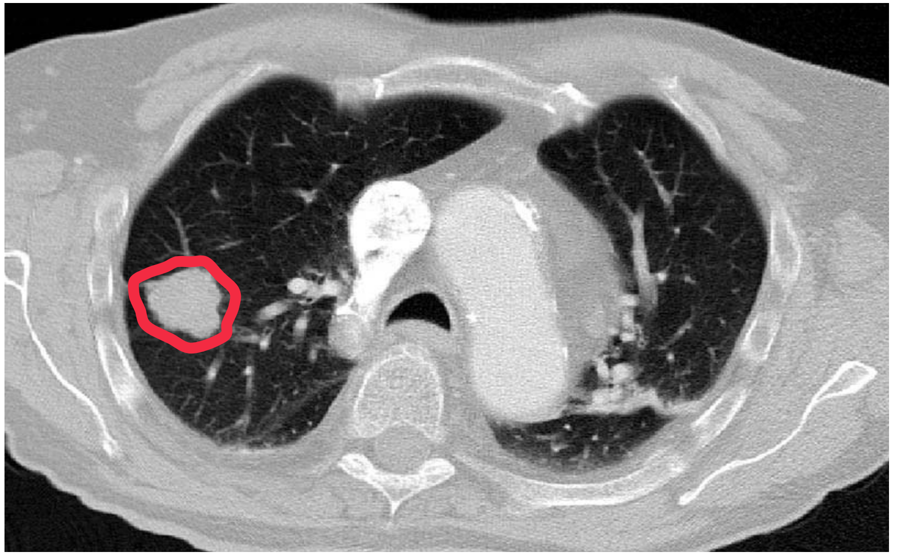
Morphology

Morphologic imaging with CT



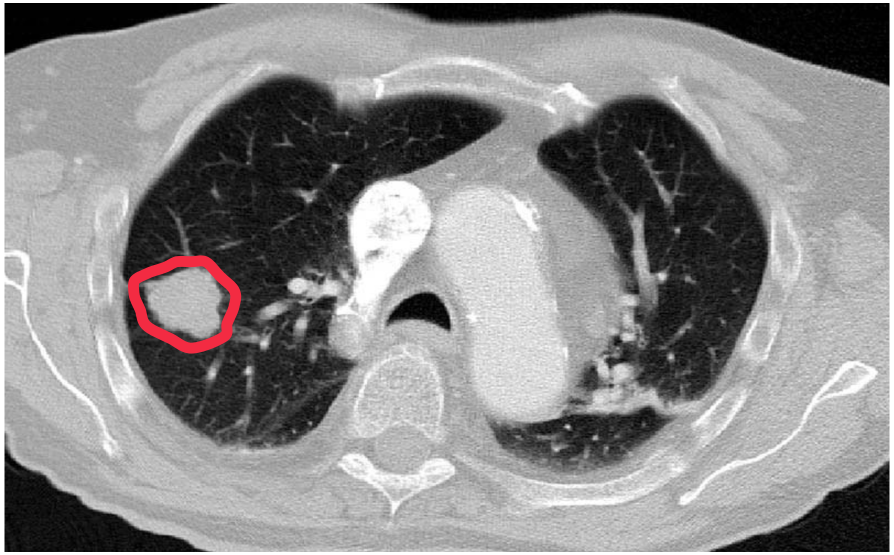
Morphology

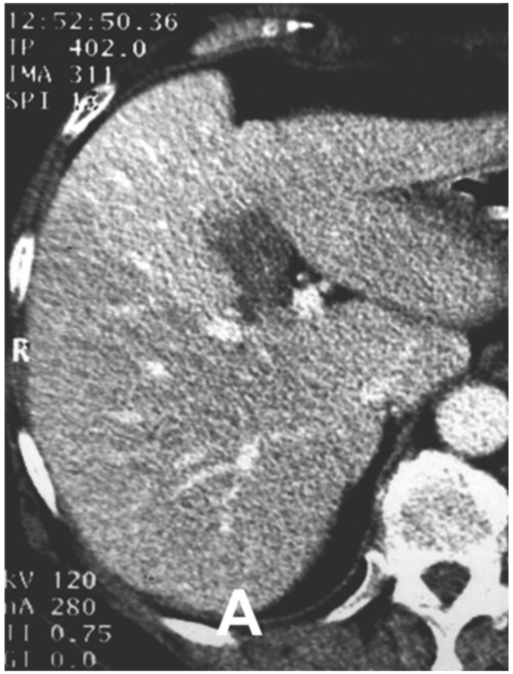
Morphologic imaging with CT



Morphology

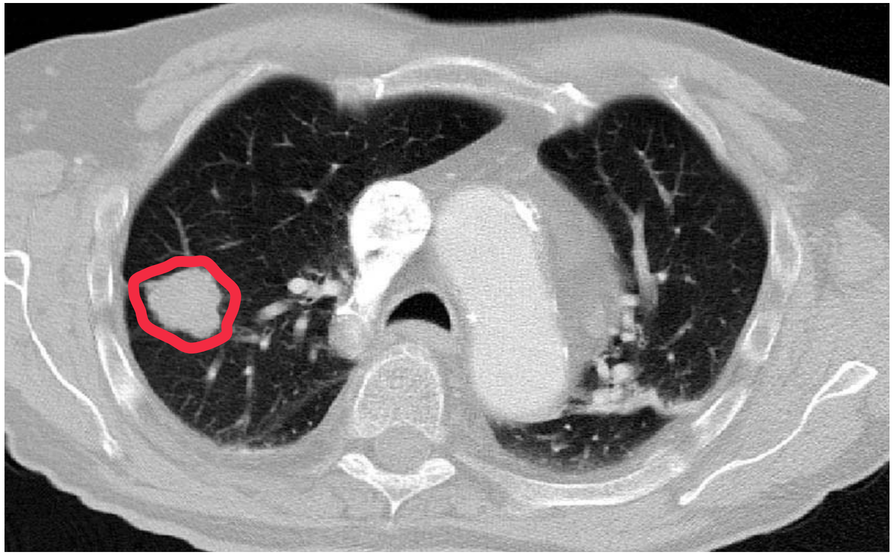
Morphologic imaging with CT





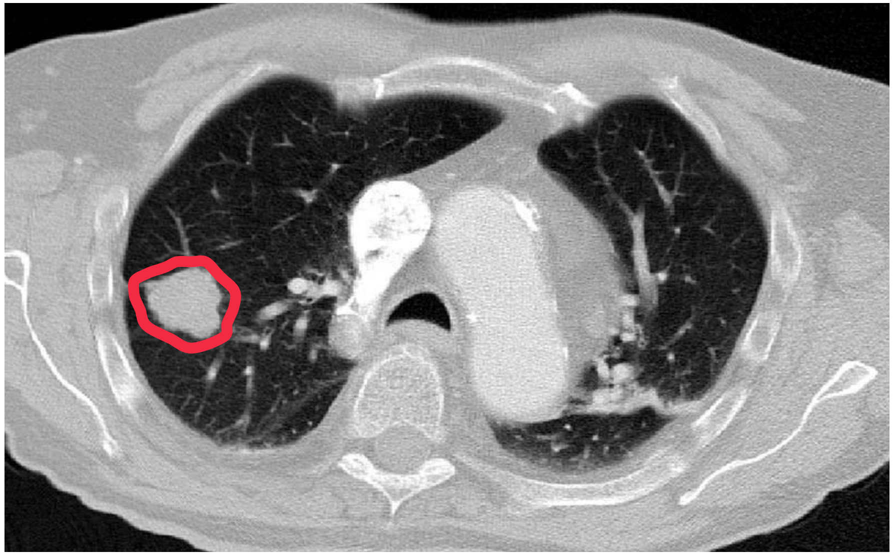
Morphology

Morphologic imaging with CT



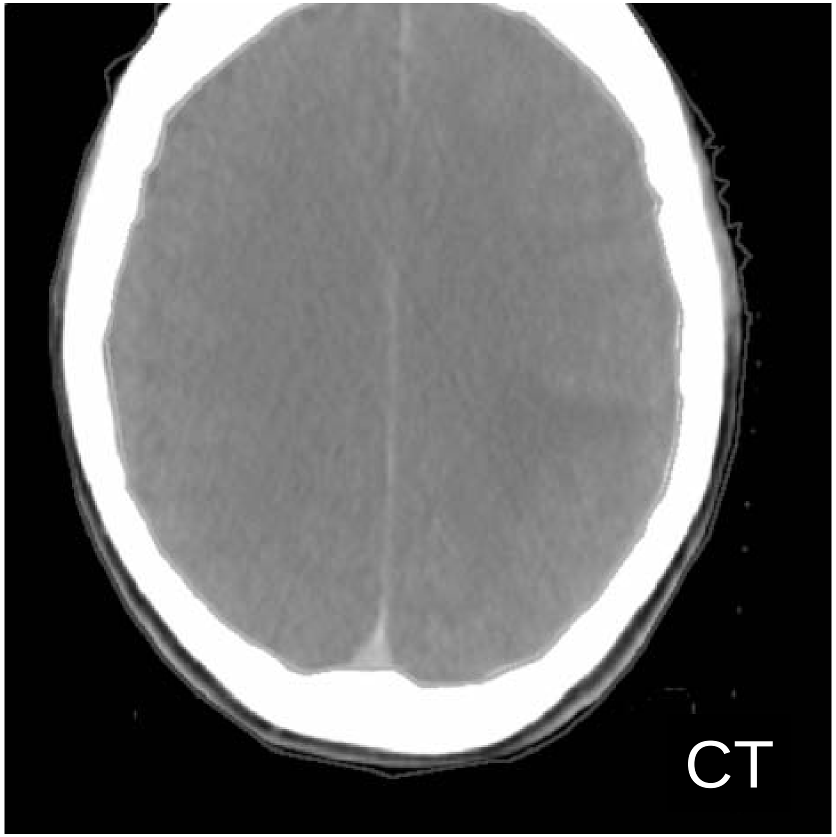
Morphology

Morphologic imaging with CT



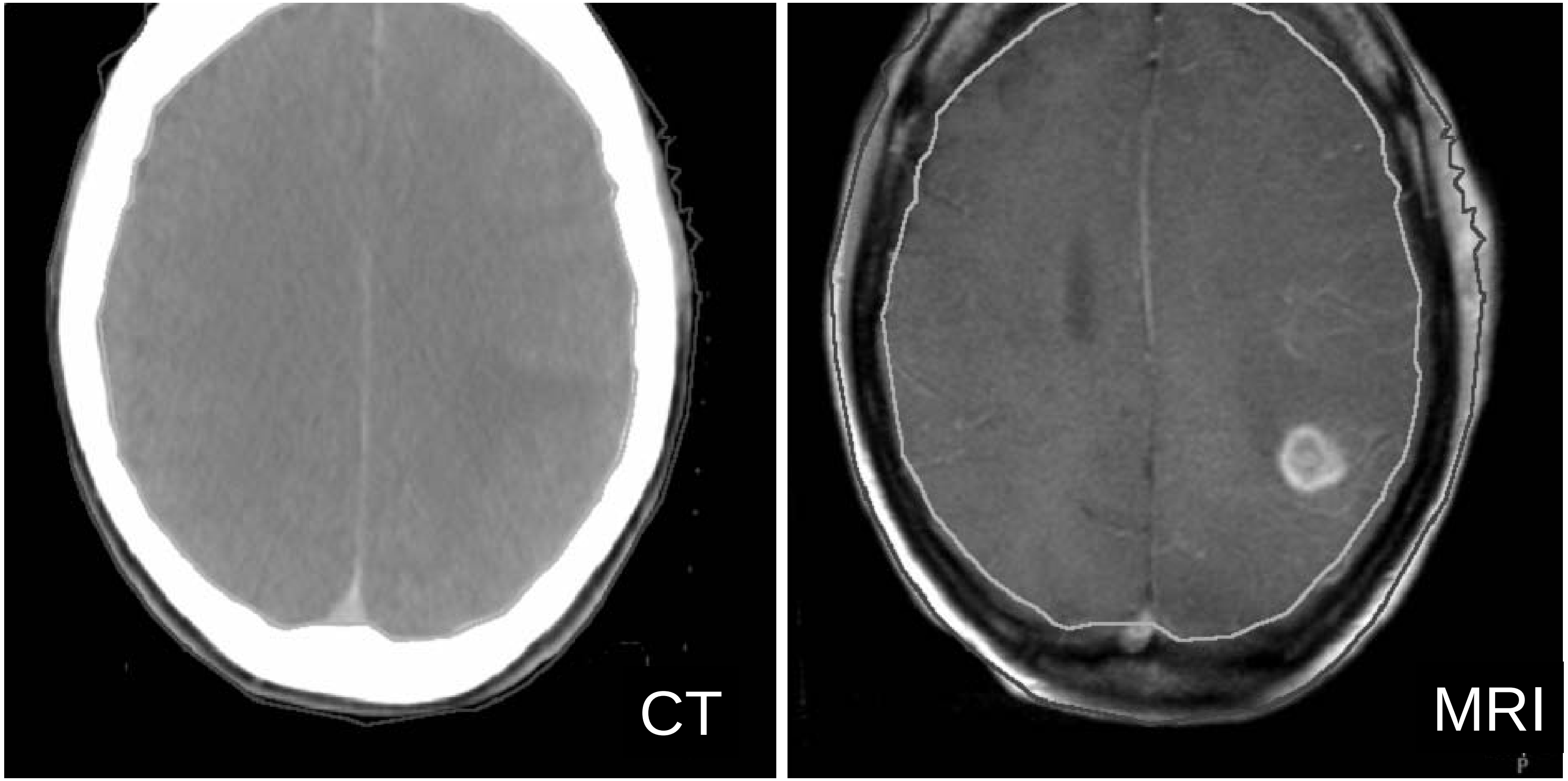
Cancer can be detected by X-ray CT,
if the tumour tissue has a lower or
higher density than surrounding tissue

Morphology



Morphology

The contribution of MRI



MRI-Brain image clearly demonstrates a lesion which is barely detectable on the CT.

Morphology

1. Detect the primary tumour
(including all tumour extensions) !

Morphology

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(including all tumour extensions) !

2. Detection of
- Involved lymph nodes
- Distant metastases

Morphology

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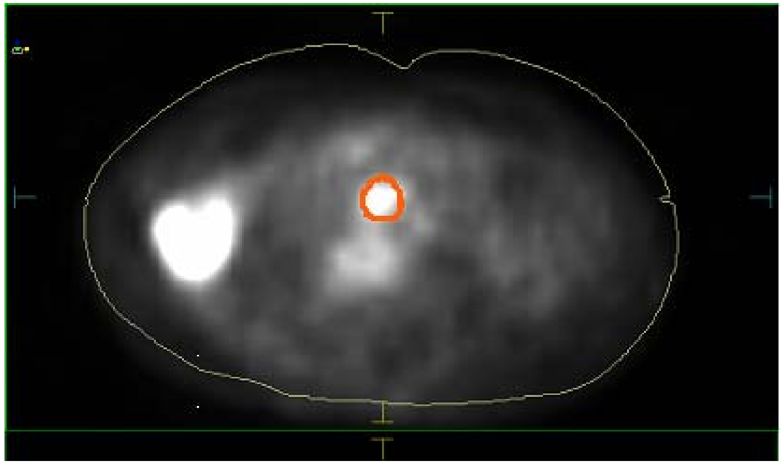
↓

Tumour staging

Morphology

Morphology

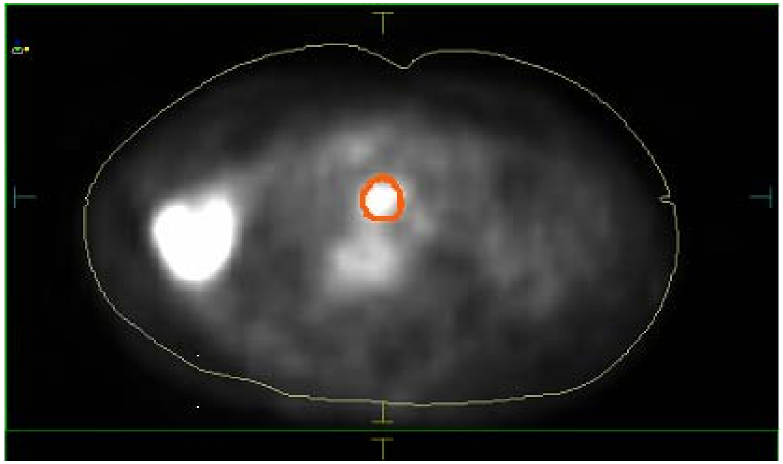


The contribution of PET

PET image showing metastases (a positive para-aortic lymph node)
Which can not be detected in CT

Morphology

The contribution of PET



PET image showing metastases (a positive para-aortic lymph node)
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Morphology

1. Detect the primary tumour
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2. Detection of

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⇩

Tumour staging

Morphology

1. Detect the primary tumour
(including all tumour extensions) !

2. Detection of
- Involved lymph nodes
- Distant metastases

⬇

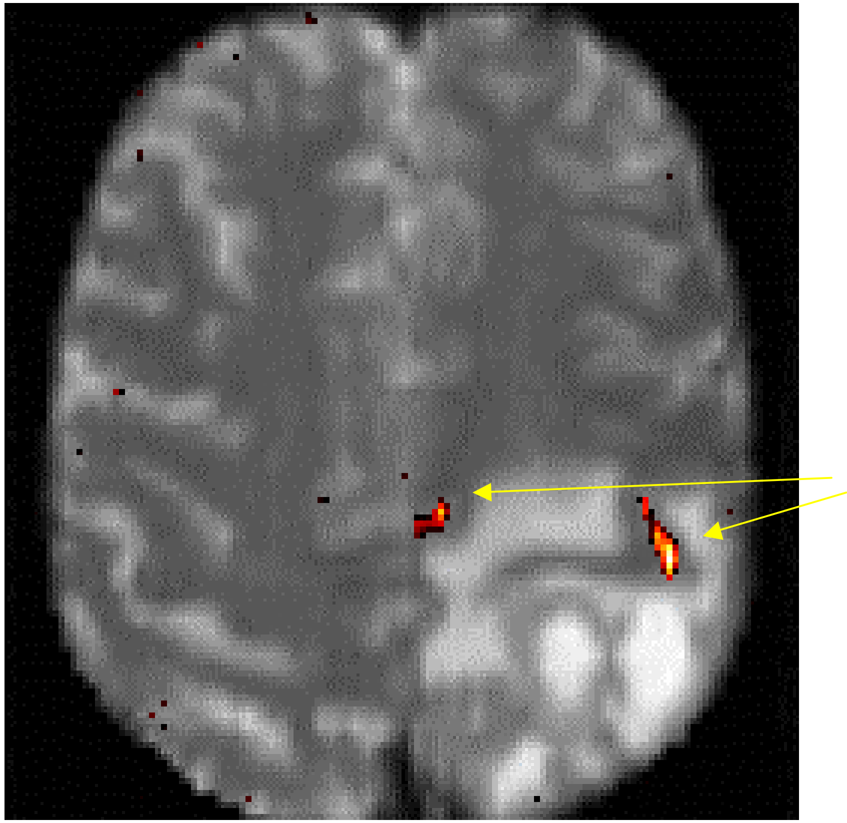
Tumour staging

3. Detect radiosensitive normal tissue
(organs at risk) !

Morphology

Imaging of
Organs at Risk

Functional
Magnetic
Resonance
Imaging
fMRI



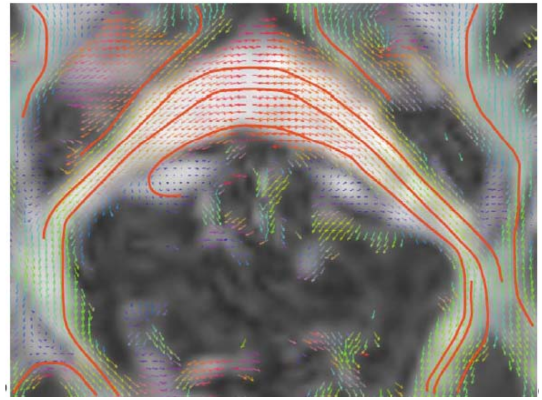
Movement
cortexes

Patient with a glioblastoma: finger tapping fMRI EPI image
(from Schad. NMR Biomed 2001;14:478-483)

Morphology

Imaging of
Organs at Risk

Diffusion
tensor
Imaging
(DTI)

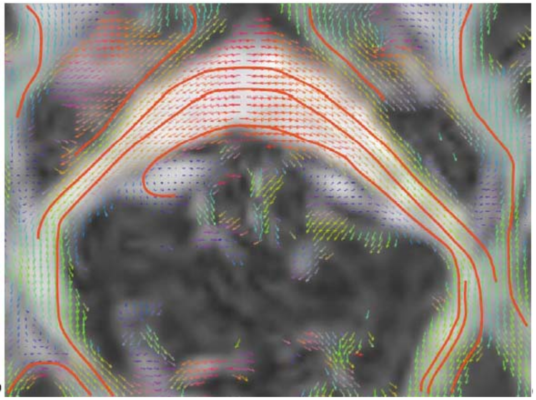


images from Stephen Correia, 2005

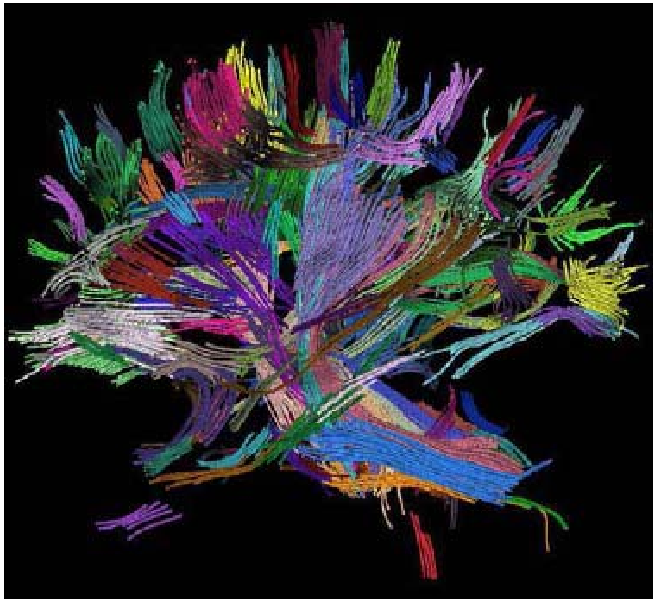
Morphology

Imaging of
Organs at Risk

Diffusion
tensor
Imaging
(DTI)



MR tractography

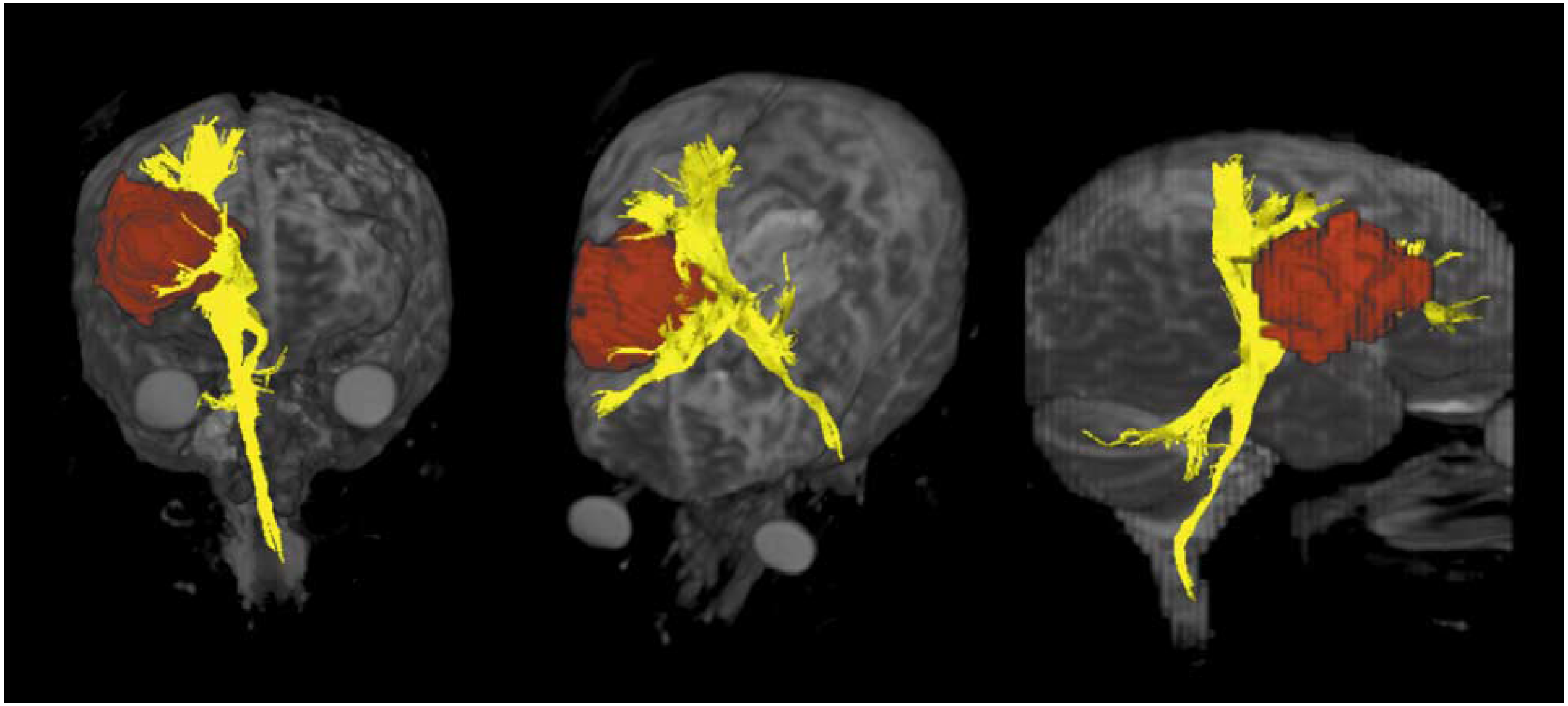


images from Stephen Correia, 2005

Morphology

Imaging of Organs at Risk

Patient with a brain tumour (glioblastoma) and white matter fiber tracts



(images from Dr. Sumu Mori, Johns Hopkins University, Baltimore)

Morphology

1. Detect the primary tumour
(including all tumour extensions) !

2. Detection of
- Involved lymph nodes
- Distant metastases

↓

Tumour staging

3. Detect neigbouring organs at risk !

Morphology

1. Detect the primary tumour (including all tumour extensions) !

2. Detection of
- Involved lymph nodes
- Distant metastases

↓

Tumour staging

3. Detect neigbouring organs at risk !

CT,
MRI

+

PET

+

CT
SPECT
fMRI

Morphology

1. Detect the primary tumour (including all tumour extensions) !

2. Detection of
- Involved lymph nodes
- Distant metastases

↓

Tumour staging

3. Detect neigbouring organs at risk !

Image fusion

CT, MRI

+

PET

+

CT
SPECT
fMRI

Movement

Movement

- How does the tumour shape and location change from day to day ?

Movement

- How does the tumour shape and location change from day to day ?

Inter-
fractional

Movement

- How does the tumour shape and location change from day to day ?
- How does the tumour change during beam delivery ?

Inter-fractional

Movement

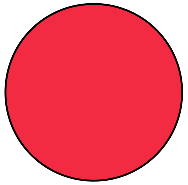
- How does the tumour shape and location change from day to day ?

Inter-fractional

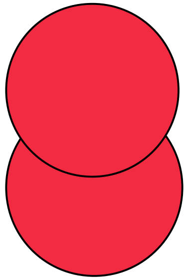
- How does the tumour change during beam delivery ?

Intra-fractional

The problem of moving tumours



The problem of moving tumours



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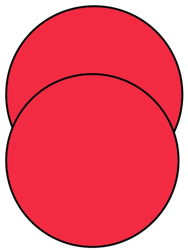

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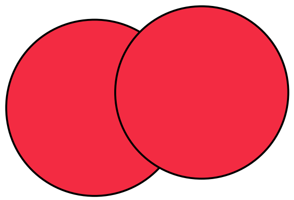

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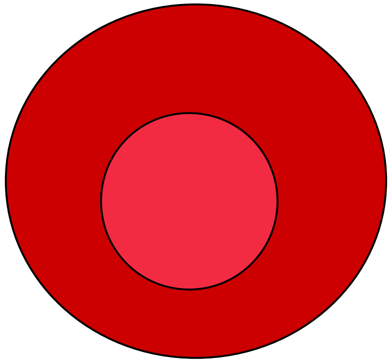
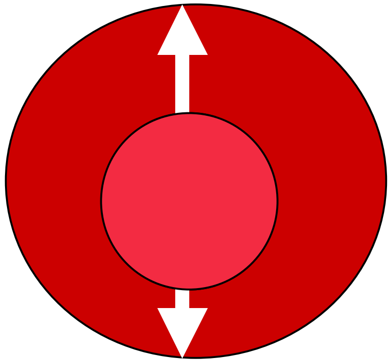


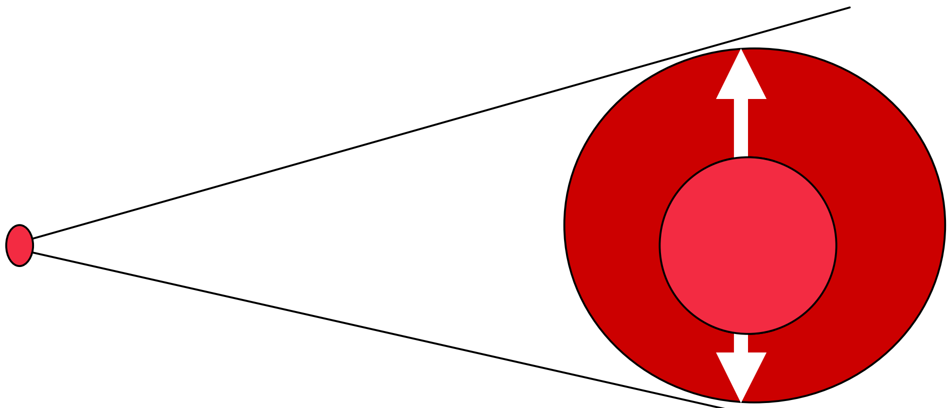
Safety margin

The problem of moving tumours

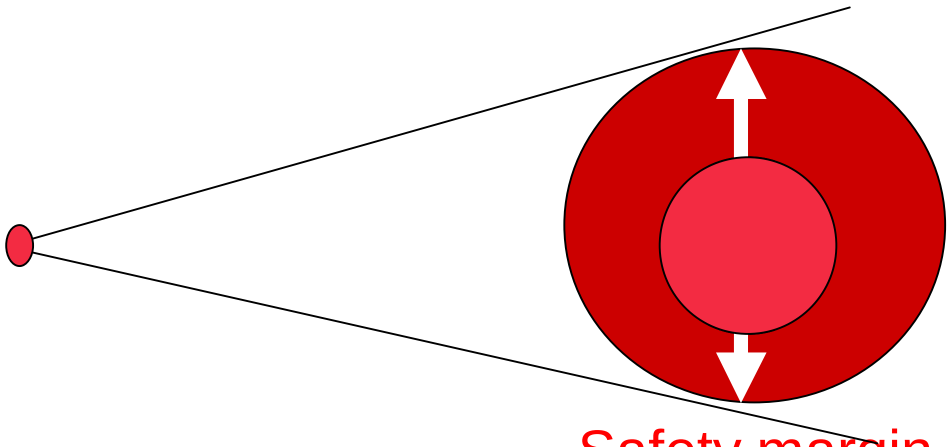


Safety margin

The problem of moving tumours



The problem of moving tumours

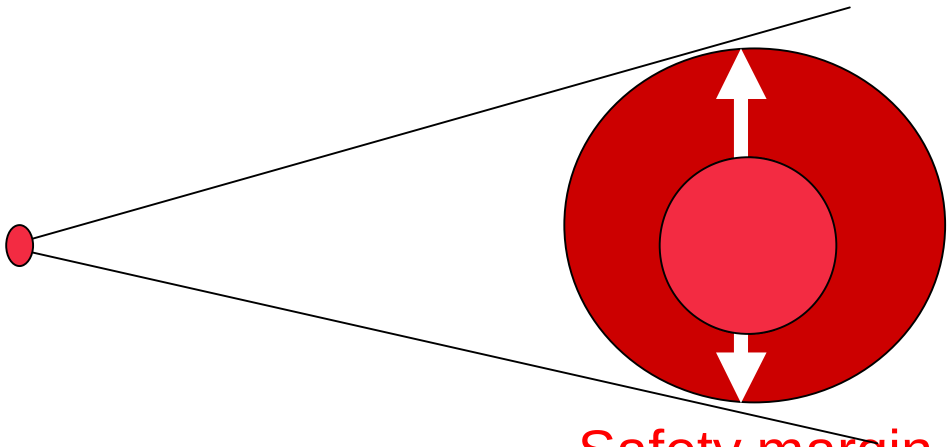


e.g.
1 cm tumour
with
3 cm movement

⬇

Irradiated volume
increases by a factor
of ~ 50 !!

The problem of moving tumours



e.g.
1 cm tumour
with
3 cm movement

↓

Irradiated volume increases by a factor of ~ 50 !!

Only 2% of the irradiated volume is tumour tissue !

Movement

Image Guided Radiotherapy/ Time adapted radiotherapy

Extension of 3D- Conformal Therapy to the 4th dimension: **time**

- Aim: Adapt treatment to patient- and organ- movements

Image Guided Radiotherapy/ Time adapted radiotherapy

Extension of 3D- Conformal Therapy to the 4th dimension: **time**

- Aim: Adapt treatment to patient- and organ- movements

Patient is treated on up to 30 days !

Image Guided Radiotherapy/ Time adapted radiotherapy

Extension of 3D- Conformal Therapy to the 4th dimension: **time**

- Aim: Adapt treatment to patient- and organ- movements

Patient is treated on up to 30 days !

Imaging of Movement

- Interfractional Imaging (day to day movement)
- Intrafractional Imaging (movement during beam delivery)

Image Guided Radiotherapy/ Time adapted radiotherapy

- CT in treatment room
- 3D Cone Beam CT integrated into a Linac
- Tomotherapy (see contribution of Rock Mackie)

Movement

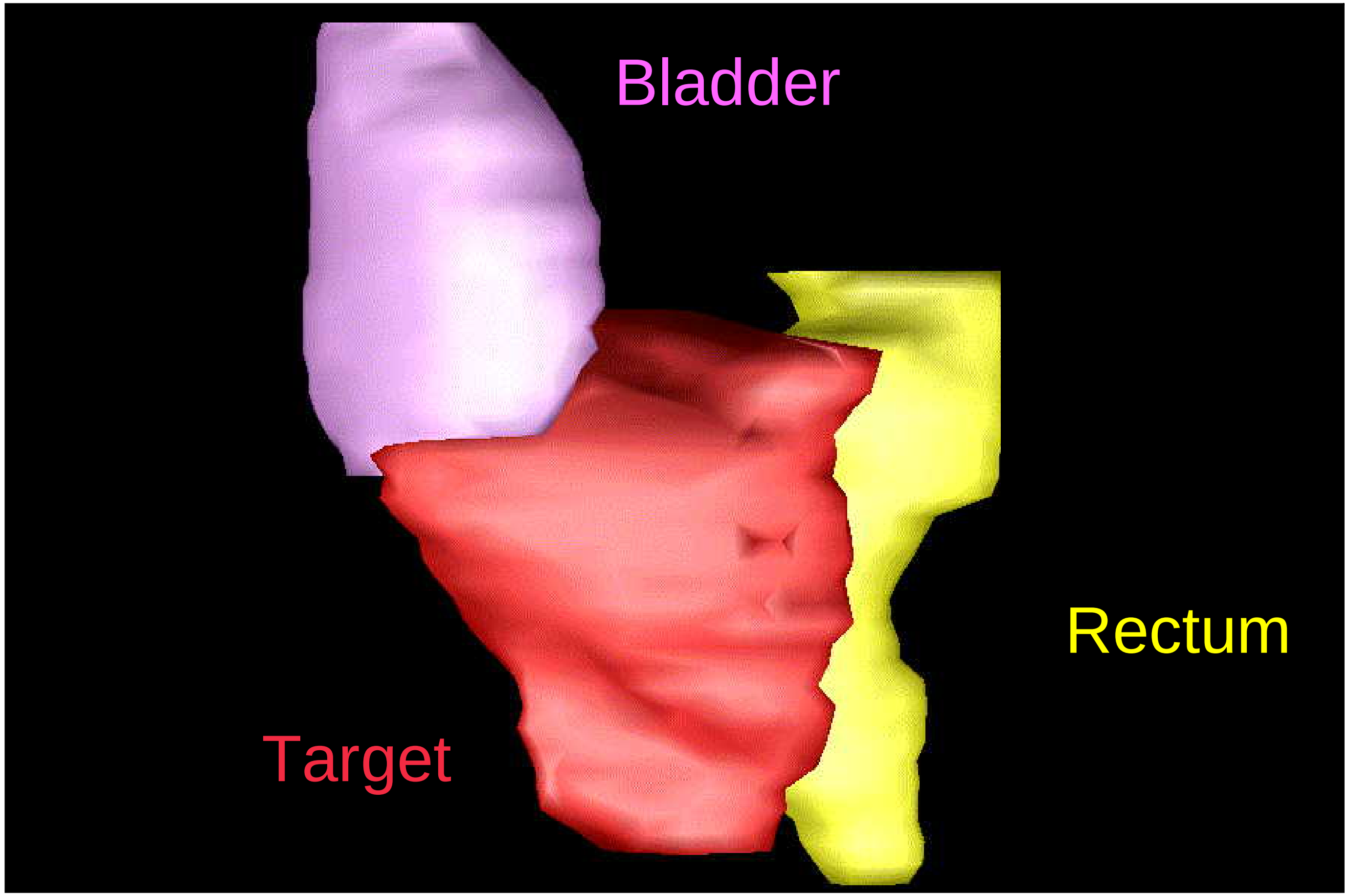
IGRT Hardware @DKFZ

In-room CT:PRIMATOM

Interfractional imaging

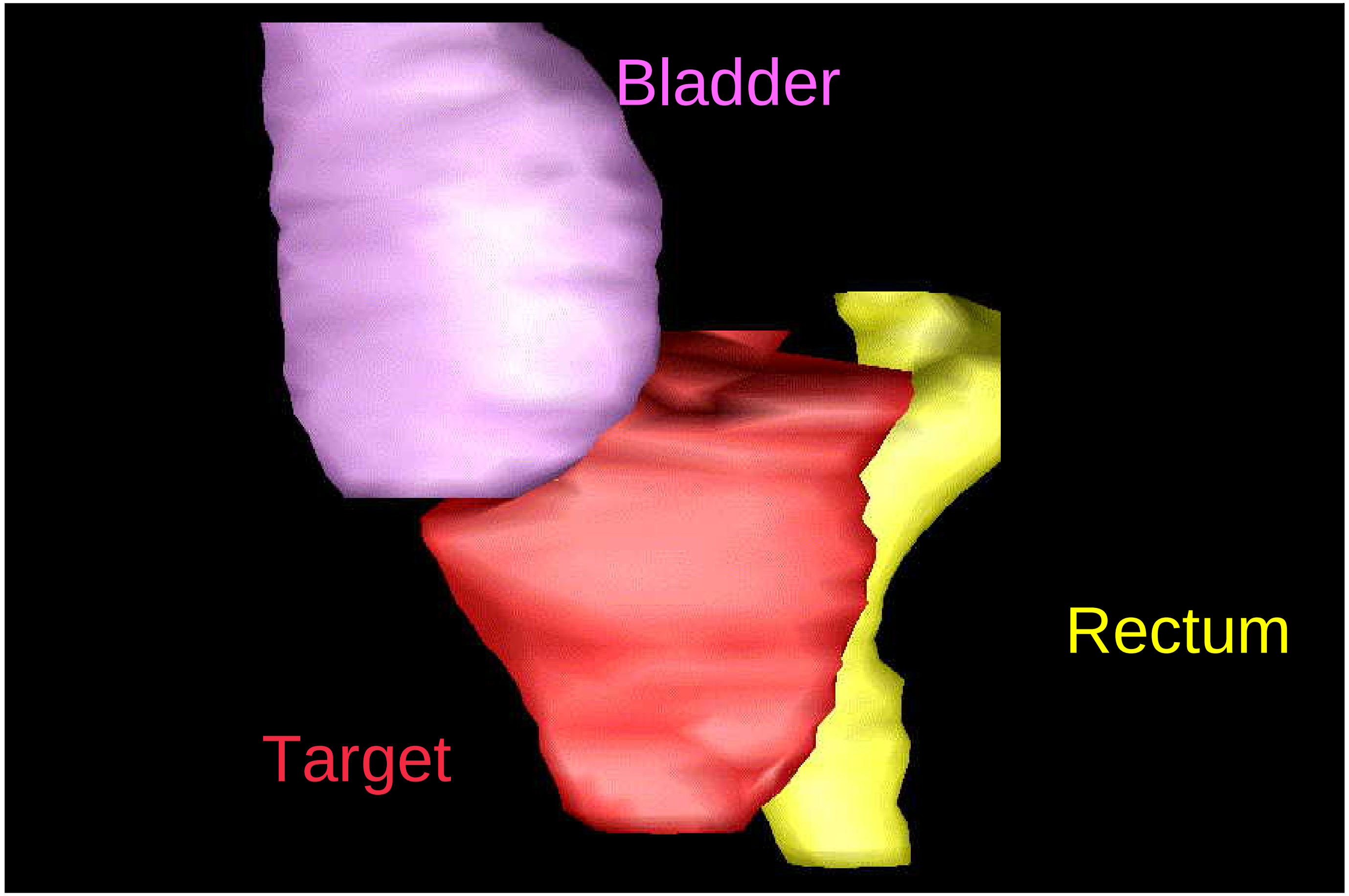
Movement

Example: Prostate – 1. Control - CT



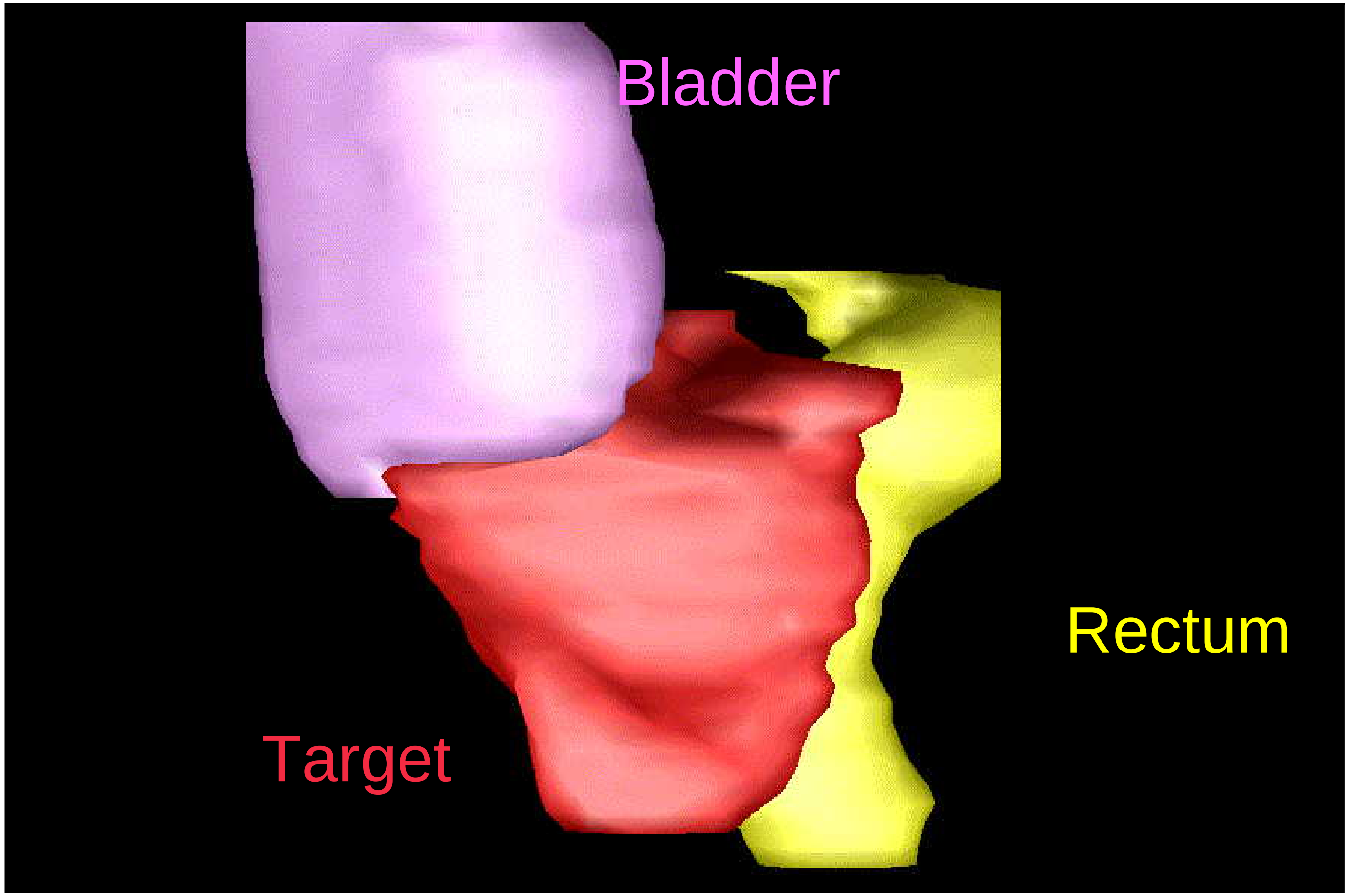
Movement

Example: Prostate – 2. Control - CT



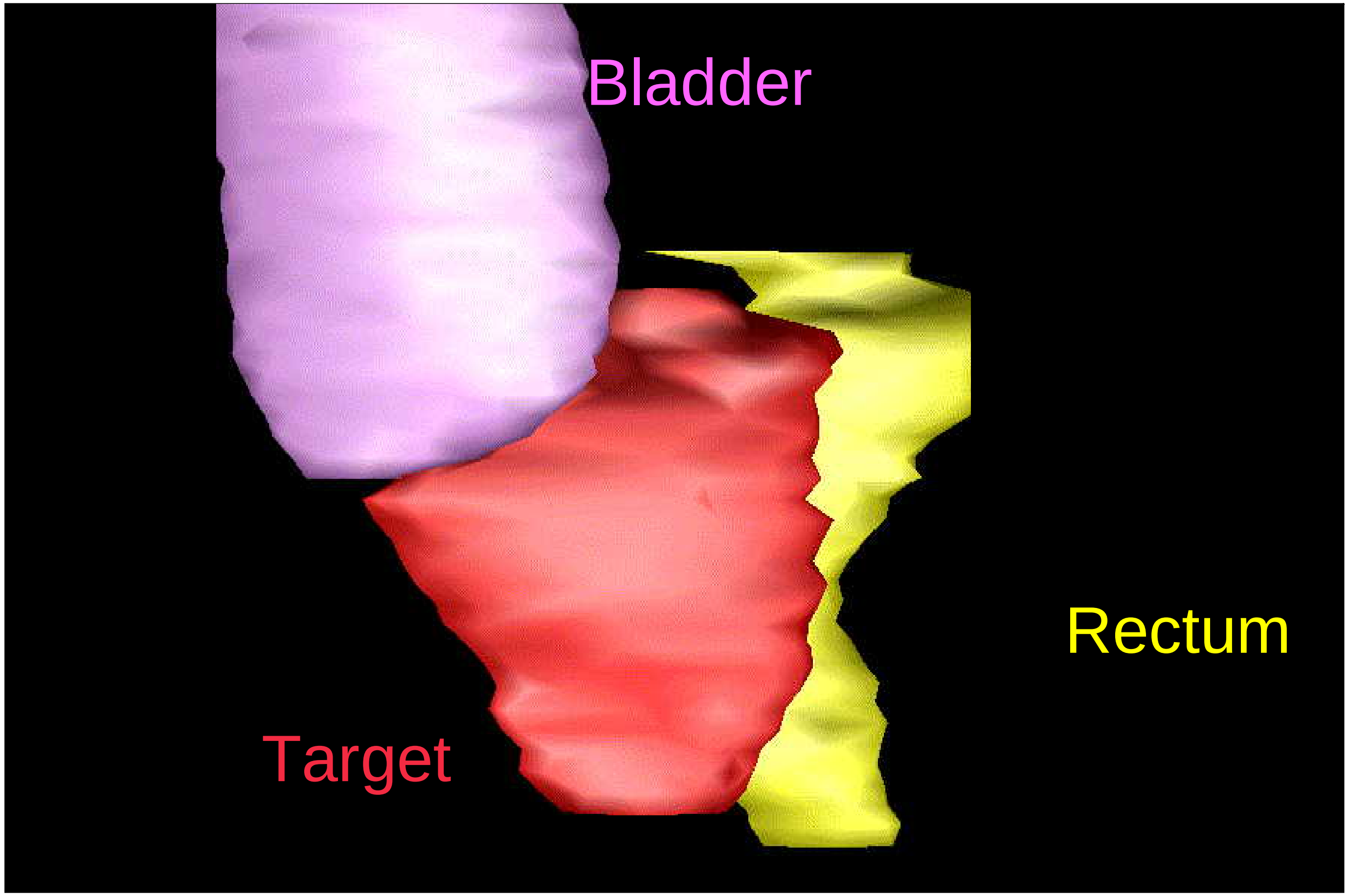
Movement

Example: Prostate – 3. Control - CT



Movement

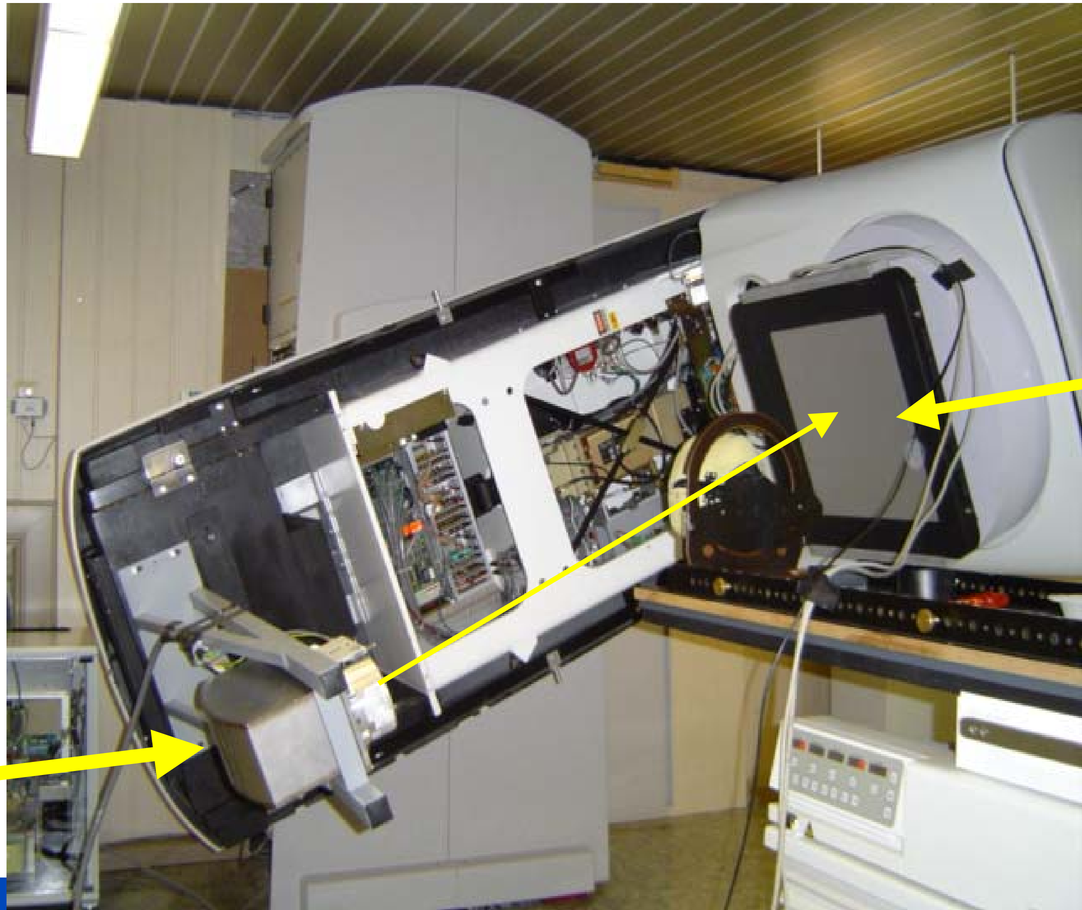
Example: Prostate – 4. Control - CT



Interfractional Movement: Paraspinal Tumor (29 CTs)

IGRT Hardware @DKFZ

- Prototype: In-line CT: PRIMUS + FPI + kV-source



ARTISTE – SMS/OCS

Interfractional Adaption

- Automatic patient positioning
  - 3D Cone Beam CT in treatment position
  - Matching with planning CT
  - Automatic determination of table shift
  - Repositioning + treatment
  - Extra time per patient: ca. 10 min.

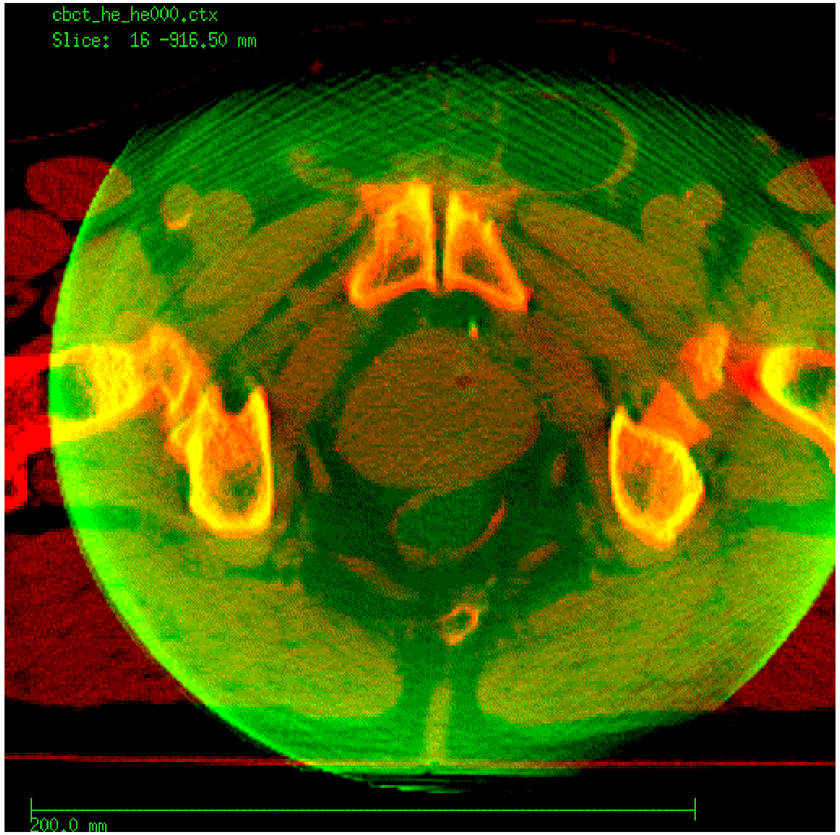
Movement

kV-CBCT Short Scan: prostate

Reconstruction of data by M. Mitschke SMS/OCS

Movement

matching with planning CT



Result: shift the patients´ couch with Δ r = (0.1, 2.7, 2.2) mm

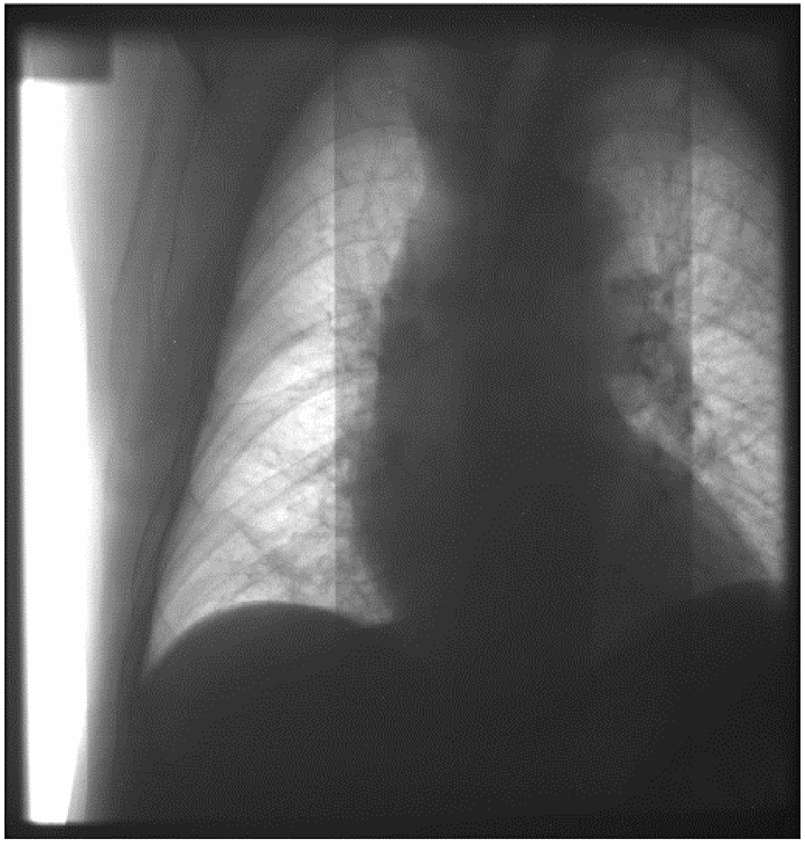
Intrafractional Adaption: Gating

- ‚Gated Irradiation‘ of moving lung tumors
  - 4D Diagnostisc CT
  - 4D Cone Beam CT
  - Gating window around exhale phase (..)

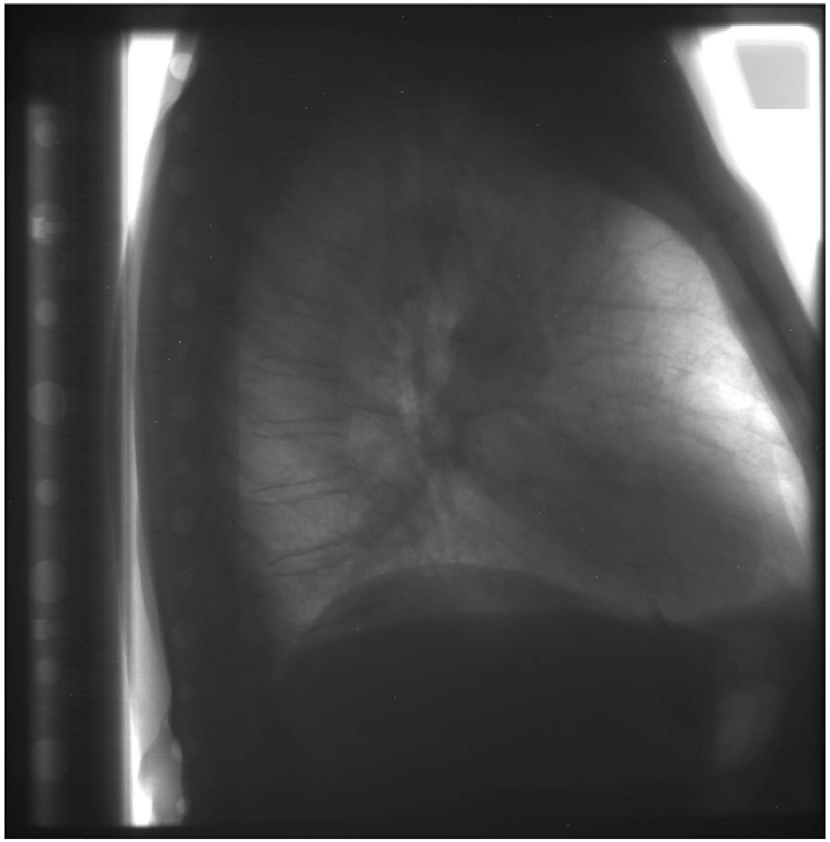
Movement

Ungated Fluoroscopy

0° Beam

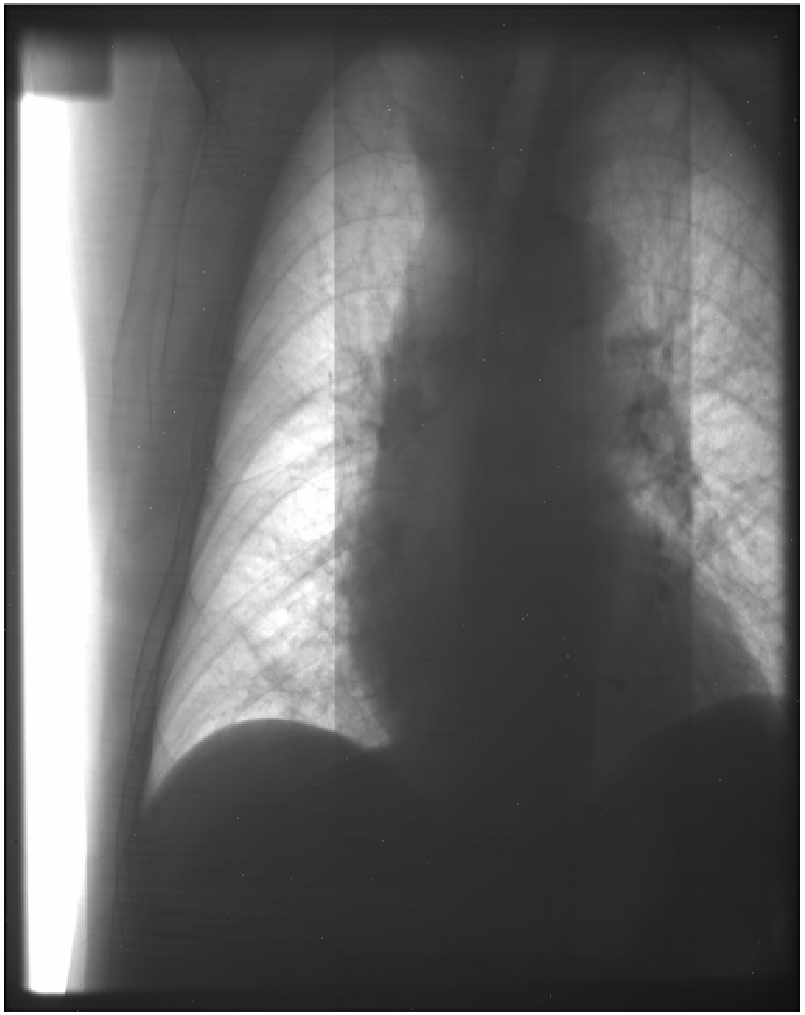


90° Beam



Movement

Gated Fluoroscopy: 0° Beam



Movement

Movement

- How does the tumour shape and location change from day to day ?

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- How does the tumour changes during beam delivery ?

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In room CT

Integrated Cone beam CT
Tomotherapy

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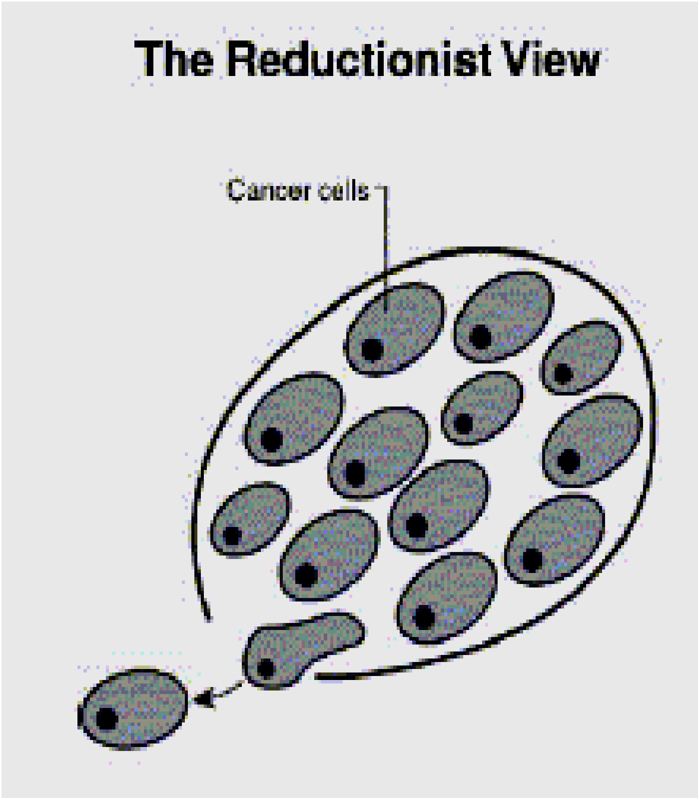
In room CT

Integrated Cone beam CT
Tomotherapy

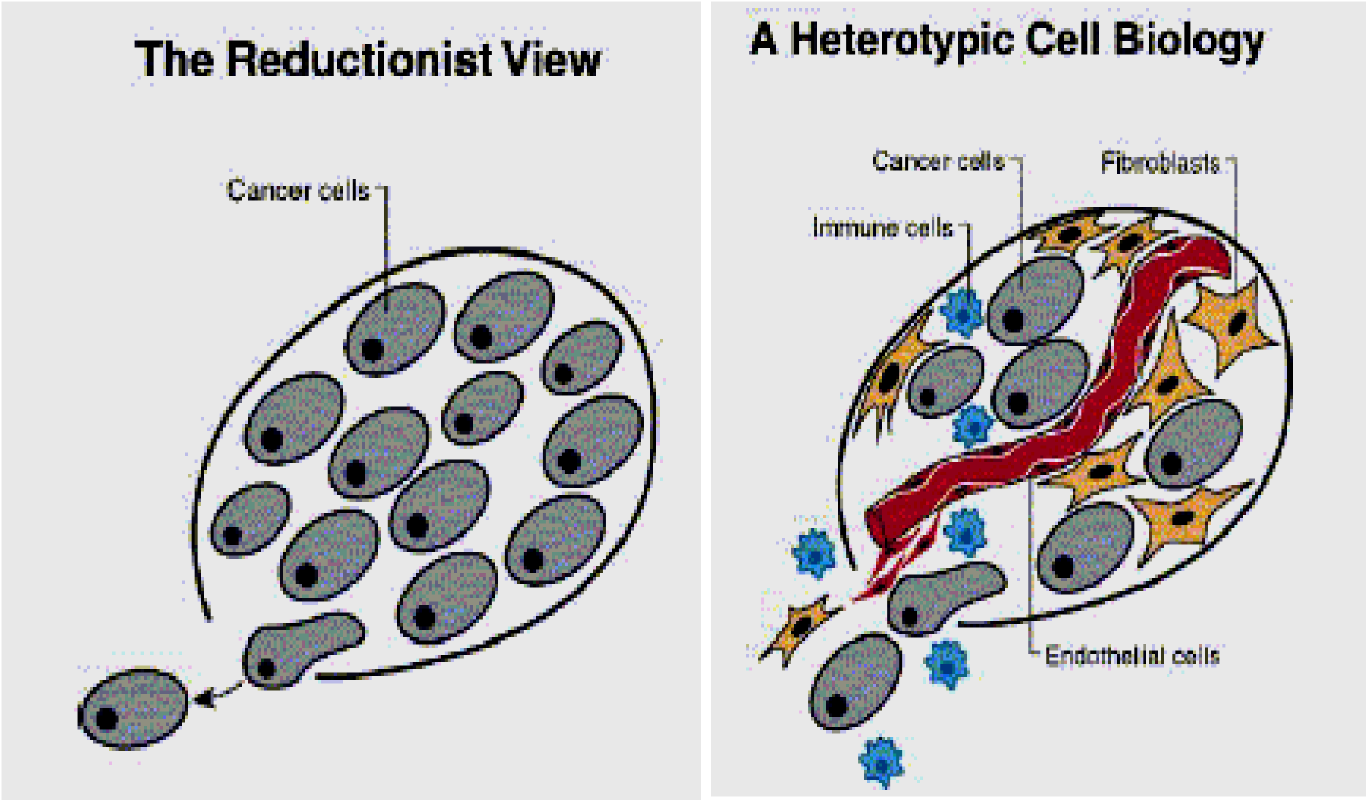
4D CT,
X-Ray Fluoroscopy
+ Markers

Biology



D. Hanaha, R. A. Weinberg, Cell,Vol. 100, 57-70,2000

Biology



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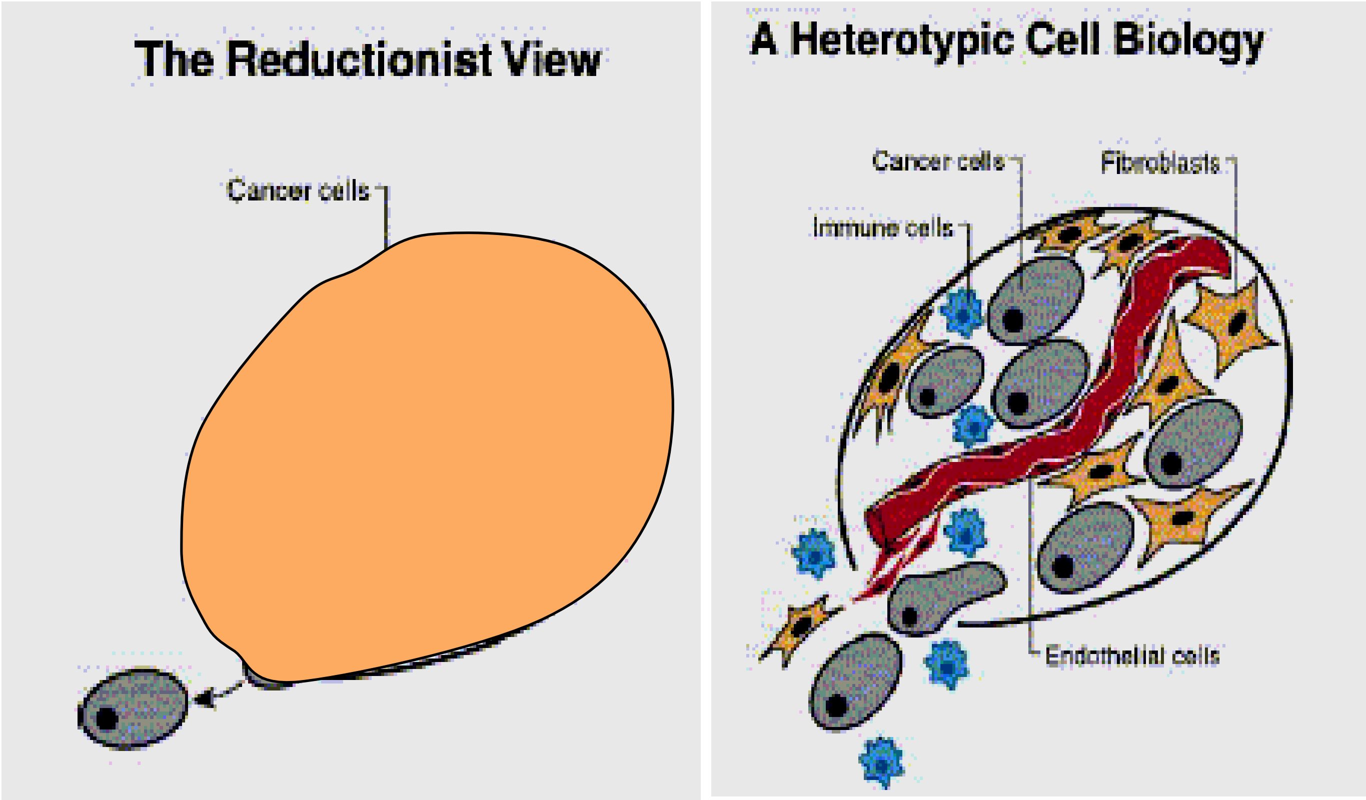

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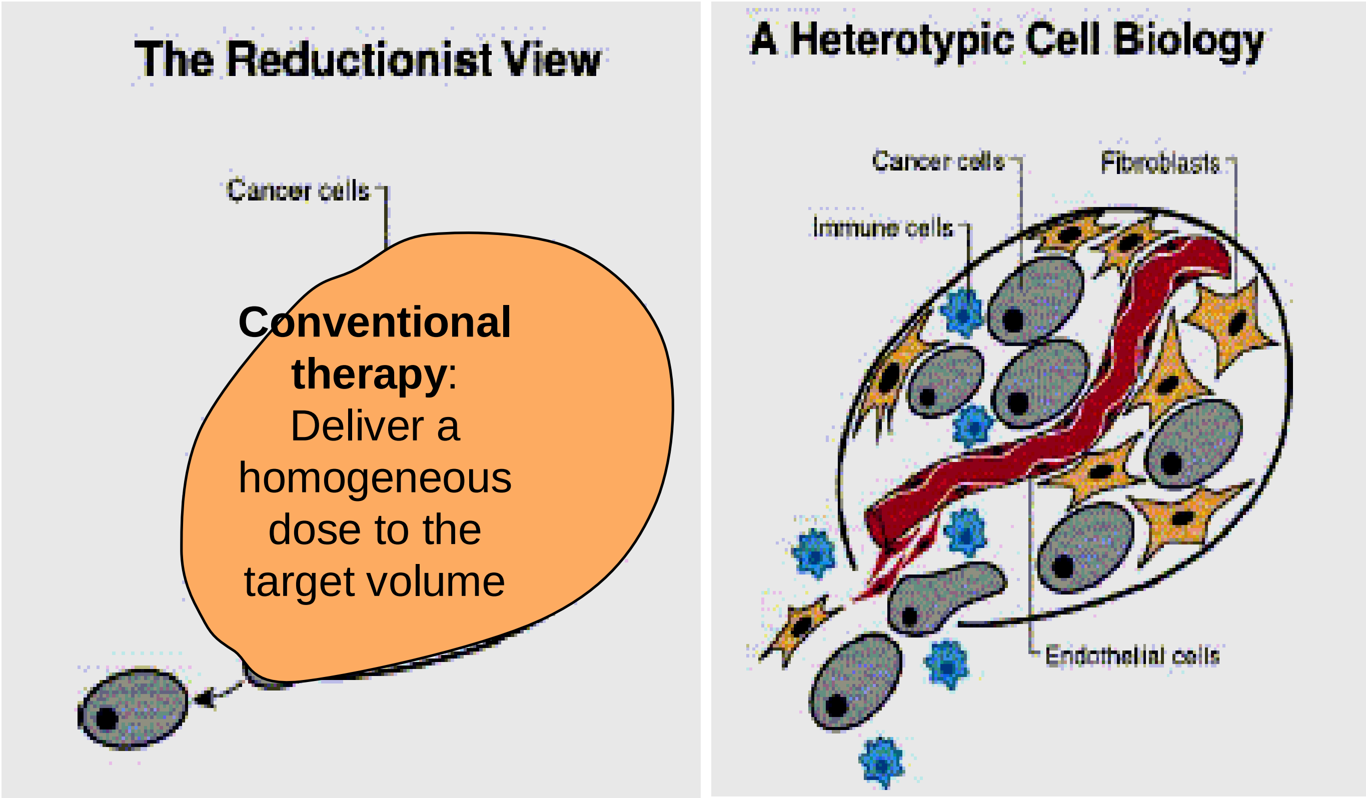

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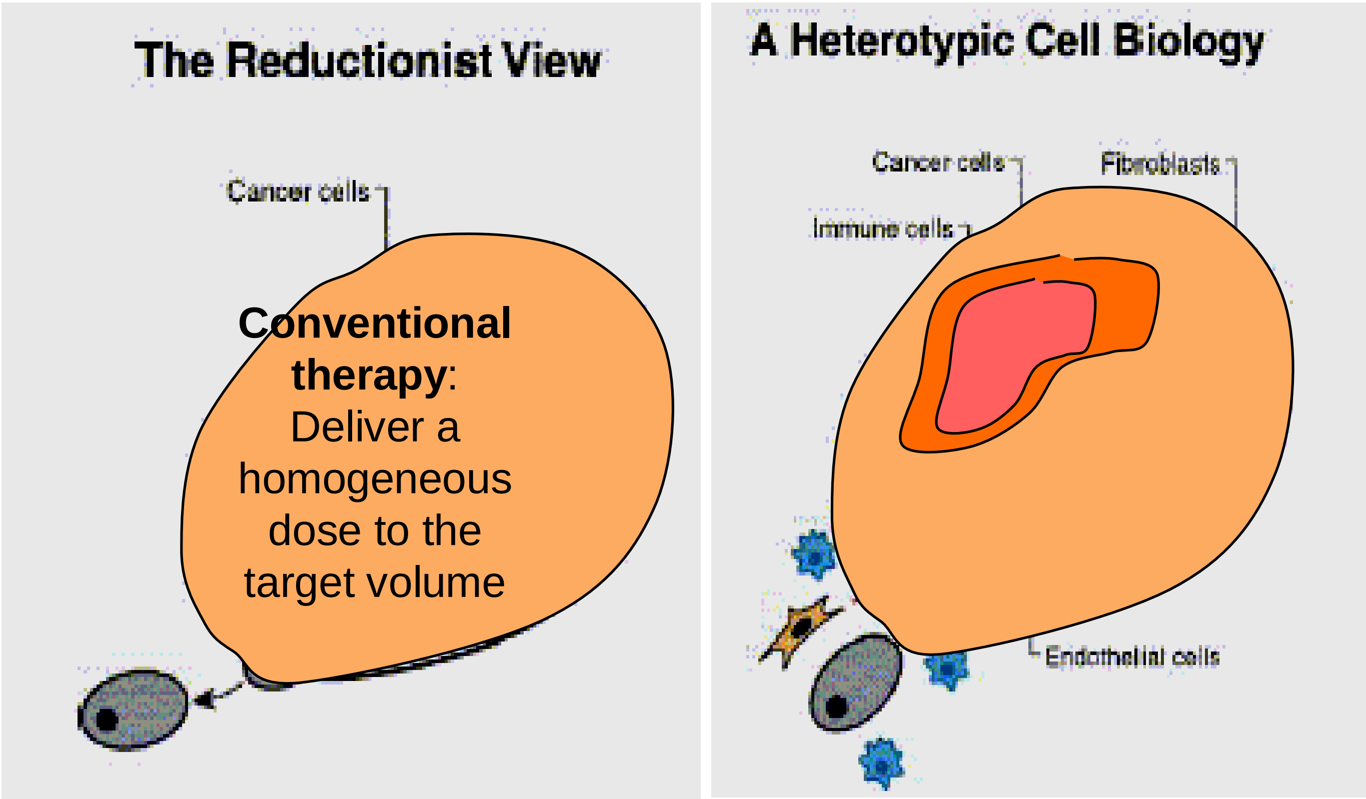

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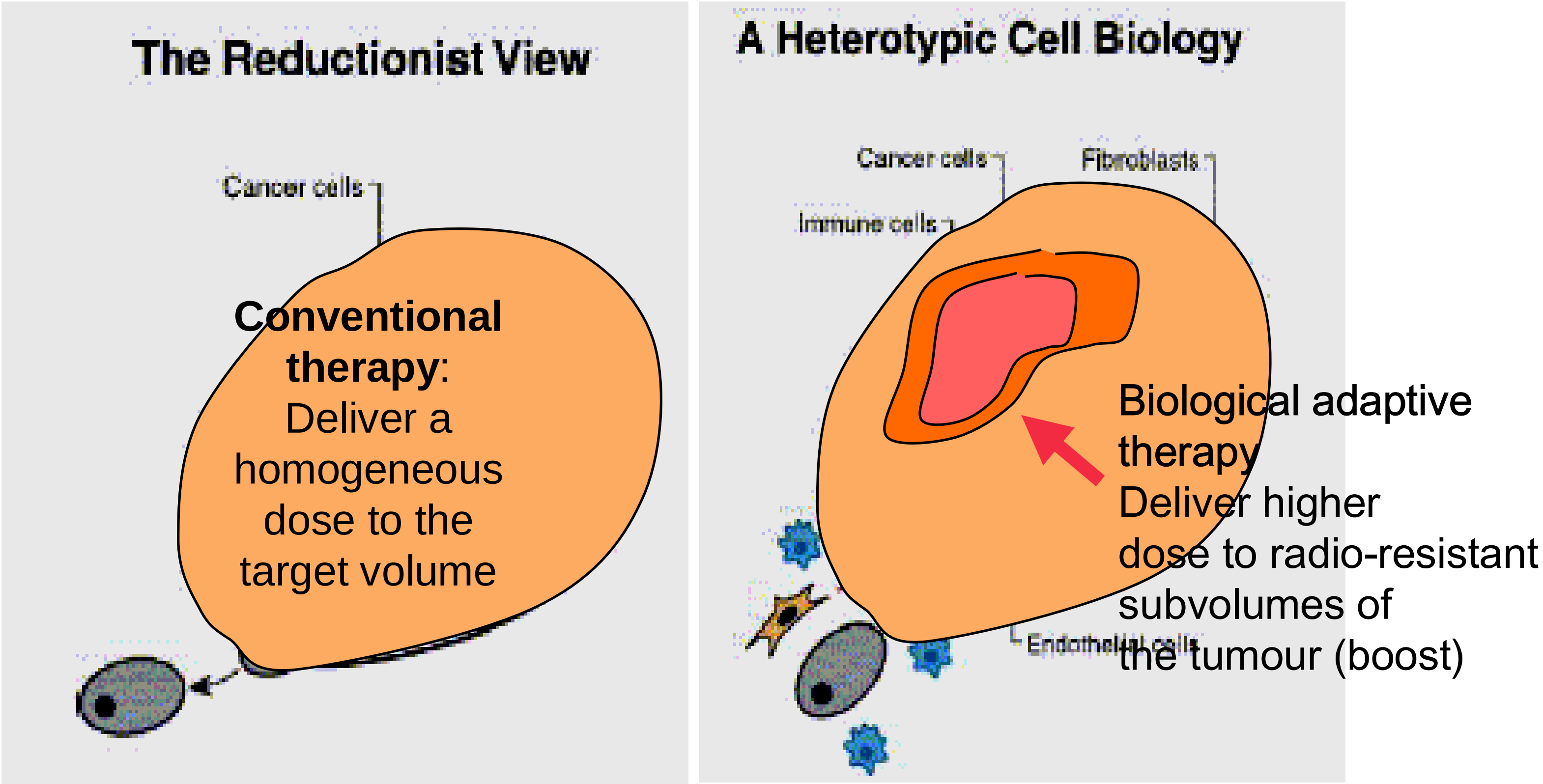


D. Hanaha, R. A. Weinberg, Cell,Vol. 100, 57-70,2000

Biology

Where are the radio-resistant areas within the tumour ?

Where are the radiosensitive areas within healthy tissue ?

Molecular Profiling

Hypoxia

Hypoxic areas within the tumour are highly radioresistant

Cellular Proliferation

Uncontrolled cellular proliferation is one of the hallmarks of malignant tumours

Apoptosis

Apoptosis („programmed cell death“) is the major form of cell death induced by radiation

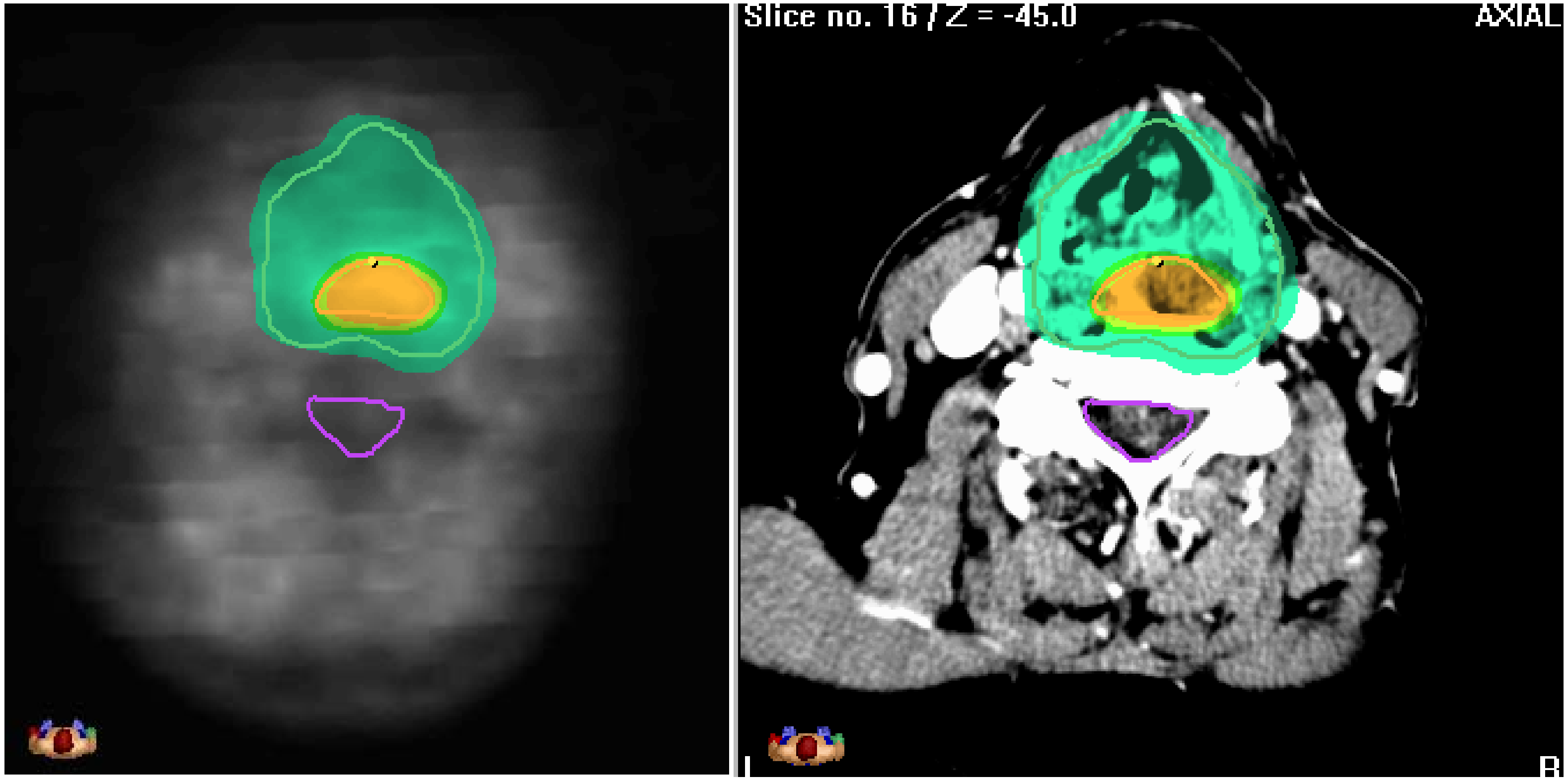
Angiogenesis

The formation of new blood vessels from pre-existing vasculature is an essential step in tumour progression and metastasis

Receptor status

Receptor molecules (growth factors and hormones) may affect radiosensitivity of tumour cells

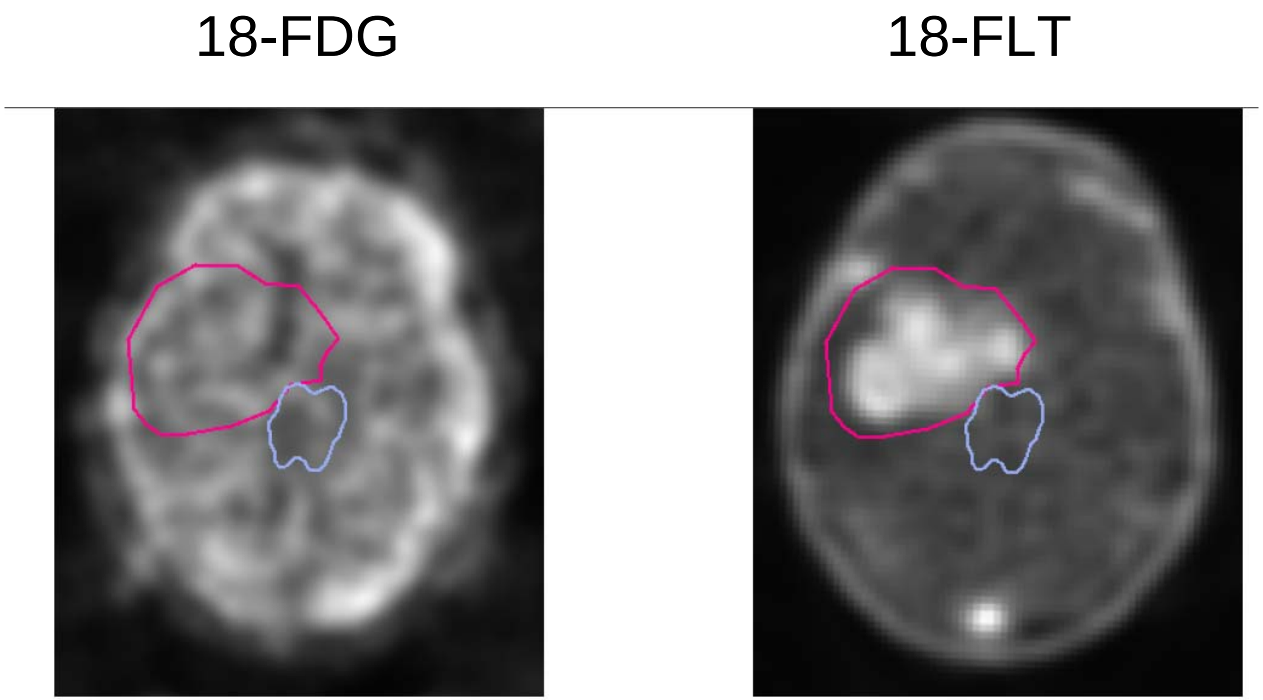
Molecular Profiling: Imaging of hypoxia with PET (18F-FAZA + CT)



Patient with a laryngeal cancer.

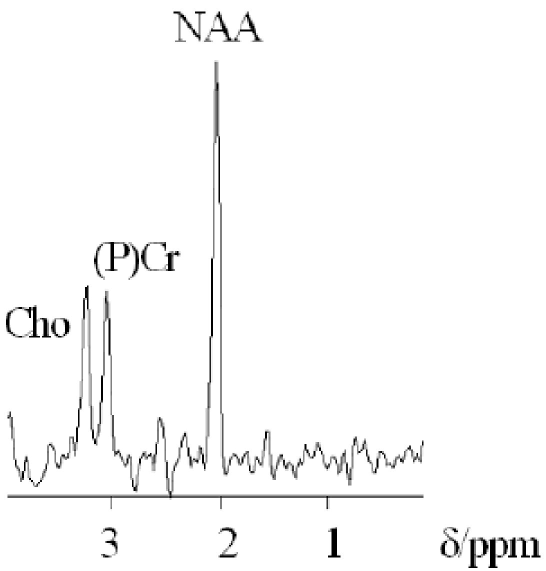
(Courtesy of Dr. M. Piert, Nuclear Medicine Department, Technical University Munich, Germany).

Molecular Profiling: Imaging of proliferation with PET (18FLT)

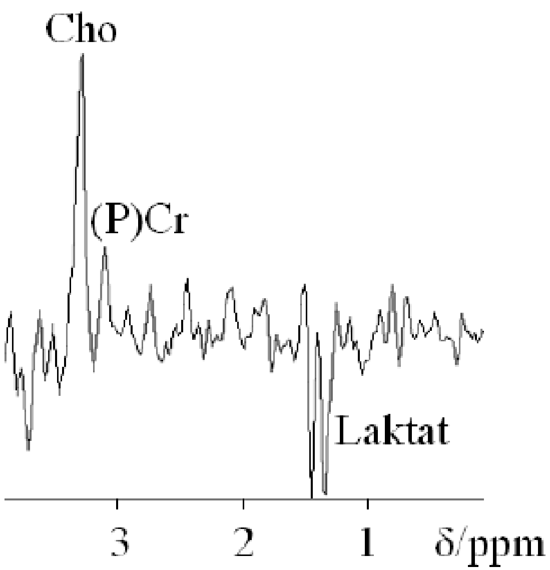


Patient with low grade glioma, PTV (pink) and
OAR (brain stem, blue) from CT-based treatment plan

Molecular Profiling: detecting proliferation with 1-H-MR-Spectroscopy

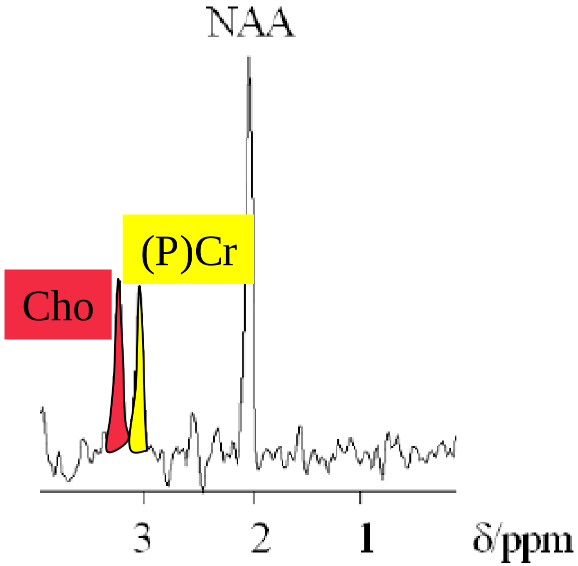


Healthy brain tissue



Brain tumour tissue

Molecular Profiling: detecting proliferation with 1-H-MR-Spectroscopy



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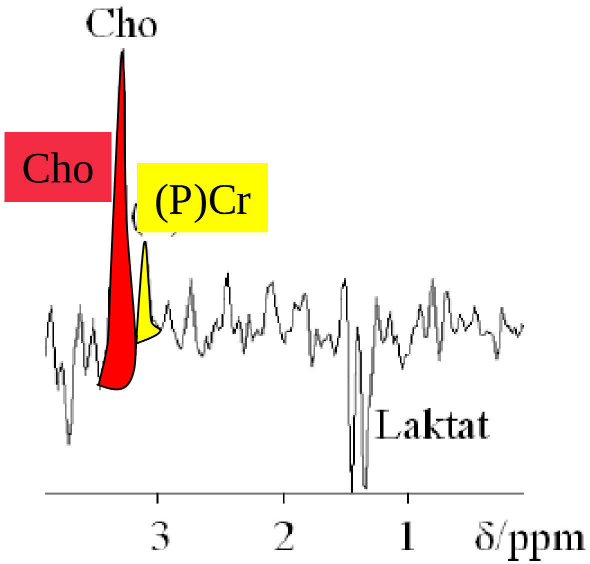

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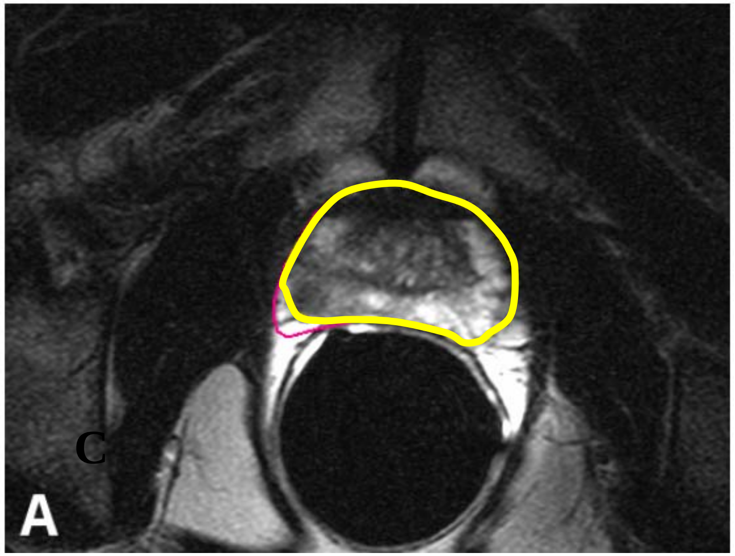
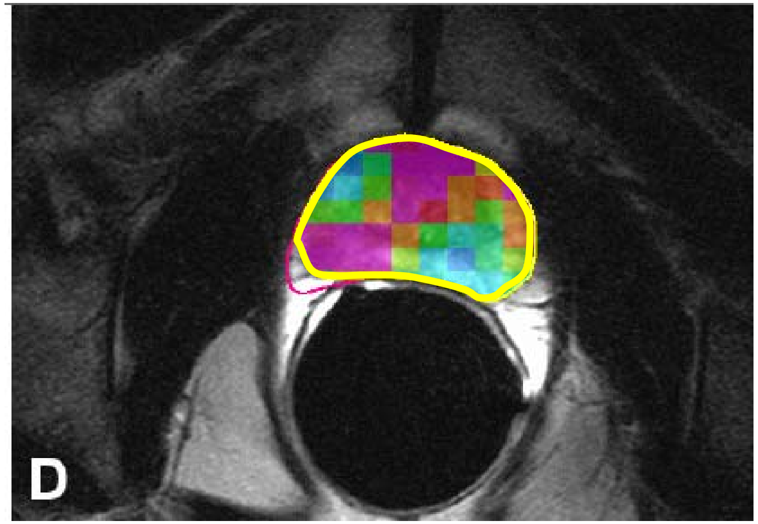
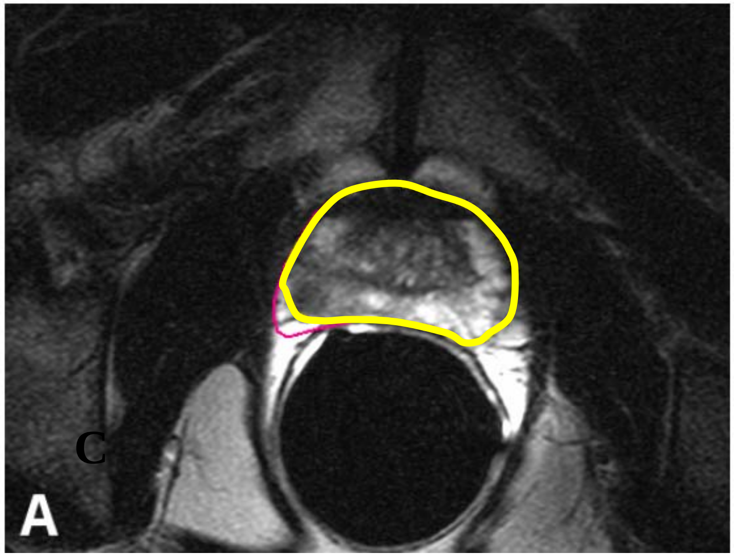


MRI: T2-Image with GTV (yellow)



GTV (yellow) +
Parameter mapping from MRS



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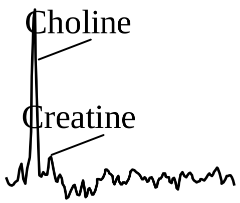

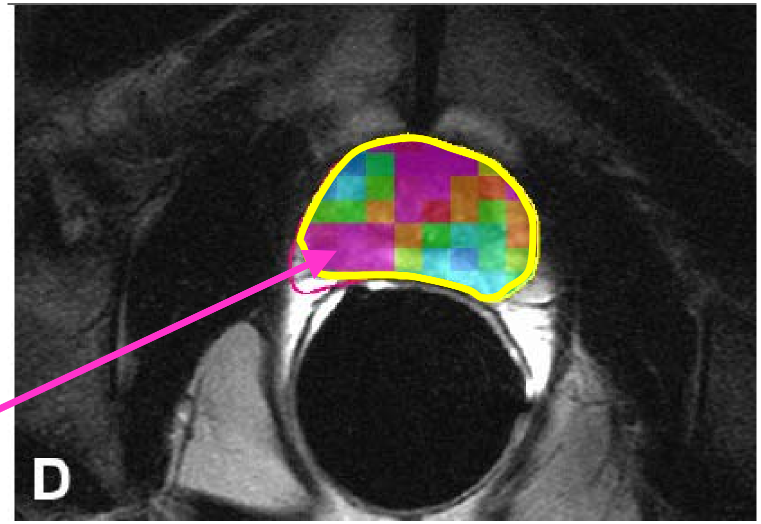

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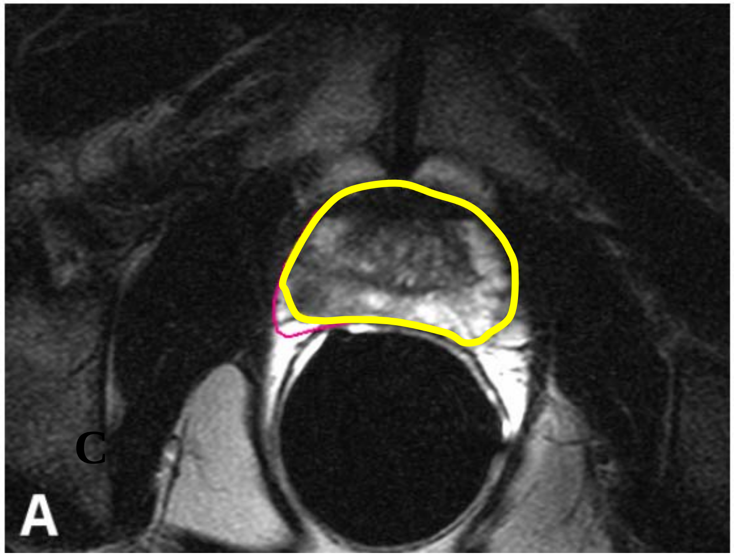

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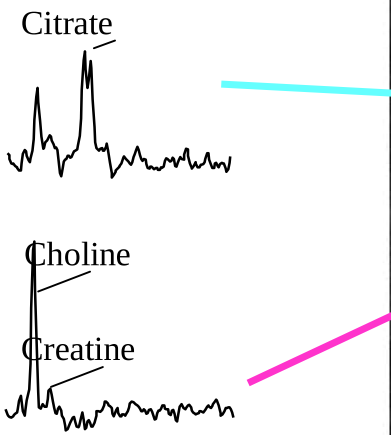

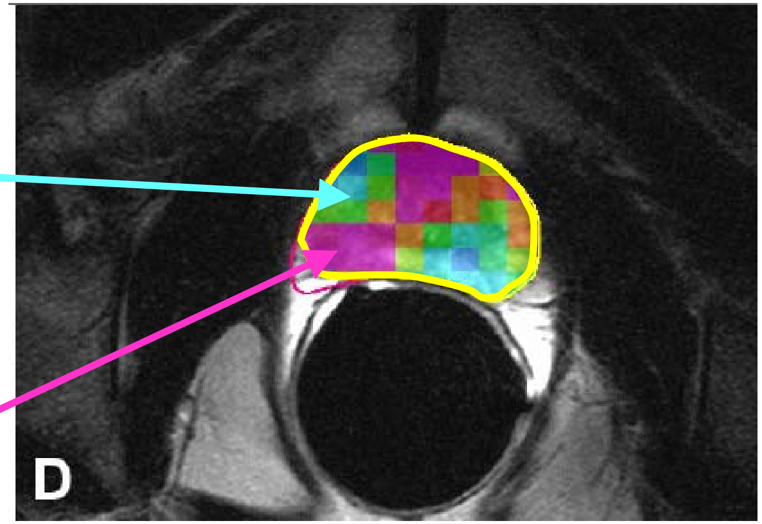

GTV (yellow) +
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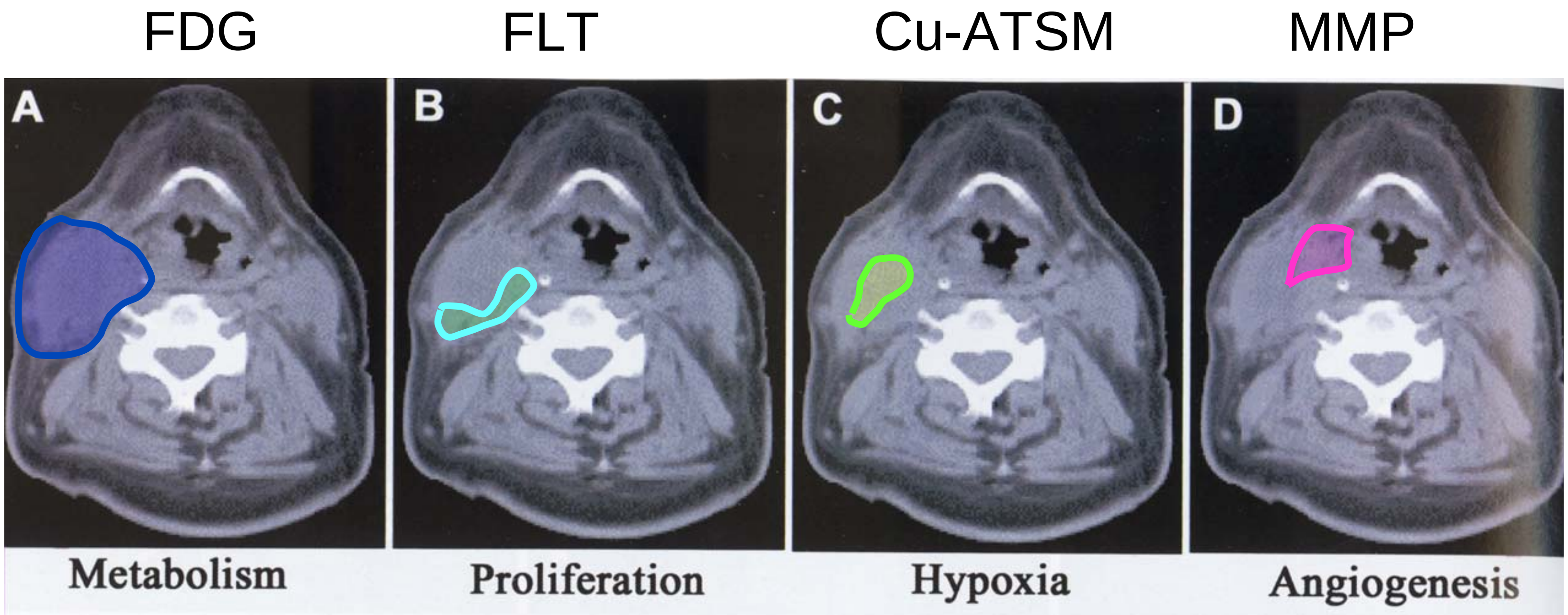
The concept of a „biological target volume“

(From
Apisanthanrax,
Rad. Res. 163, 2005)

The concept of a „biological target volume“



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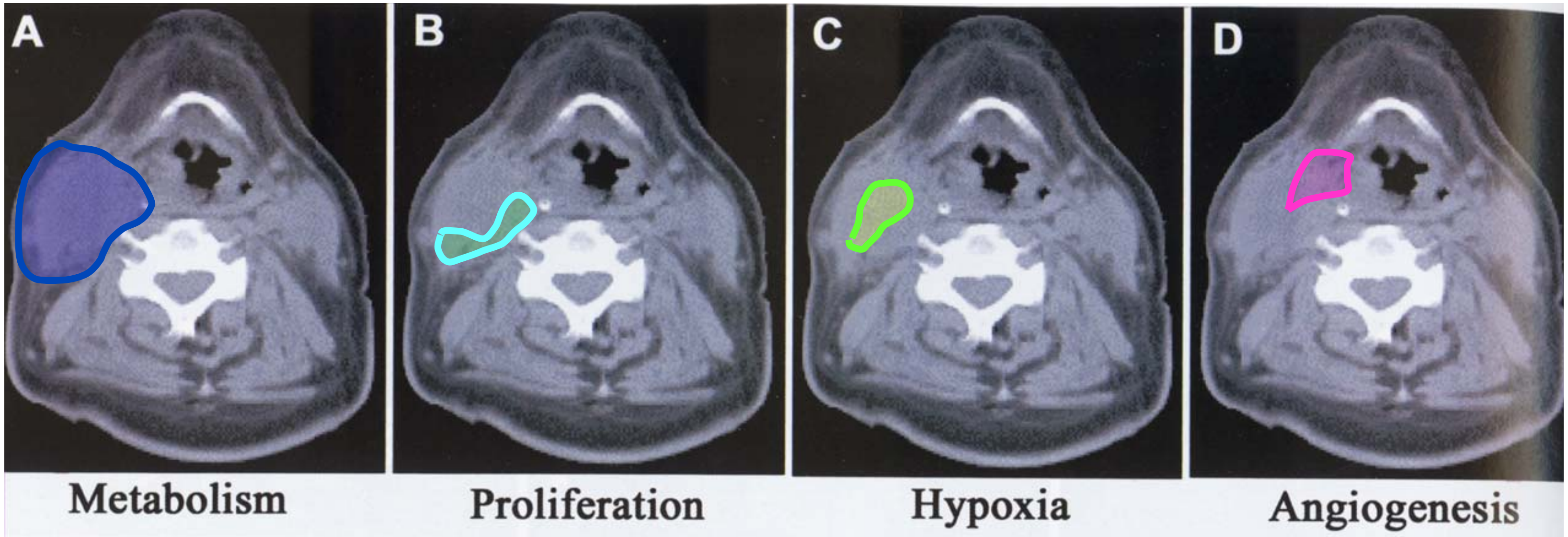
The concept of a „biological target volume“

FDG FLT Cu-ATSM MMP



+ CT

(From Apisanthanrax, Rad. Res. 163, 2005)

The concept of a „biological target volume“

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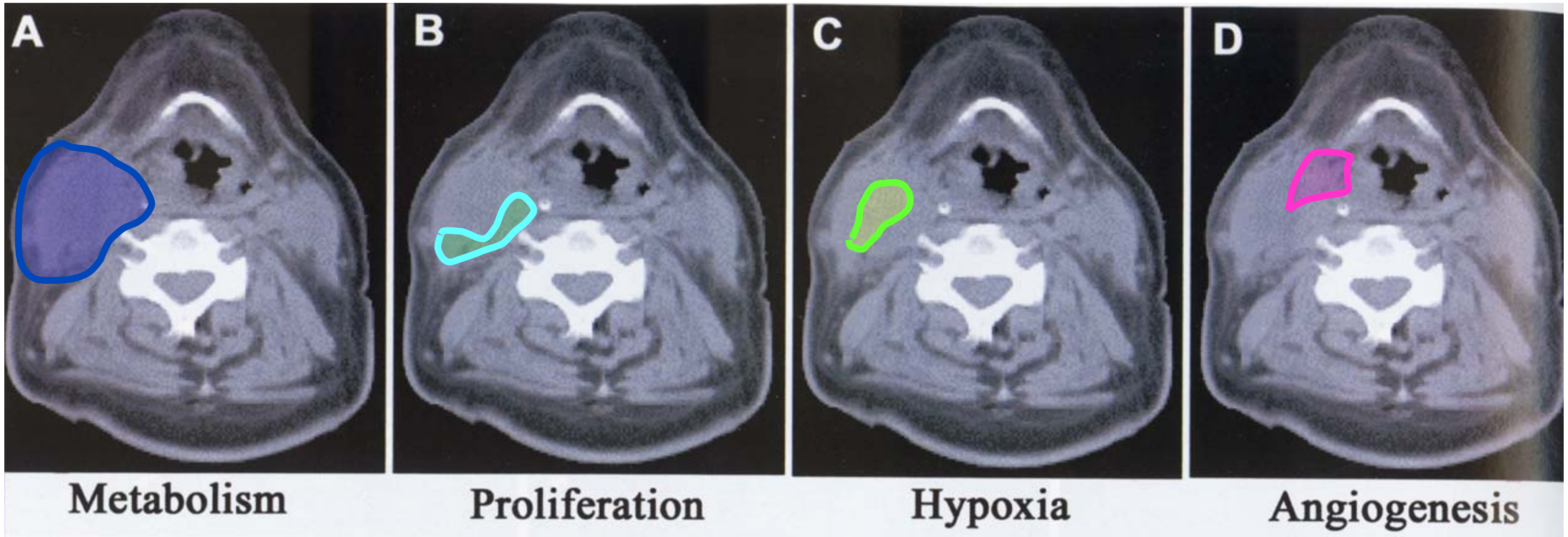

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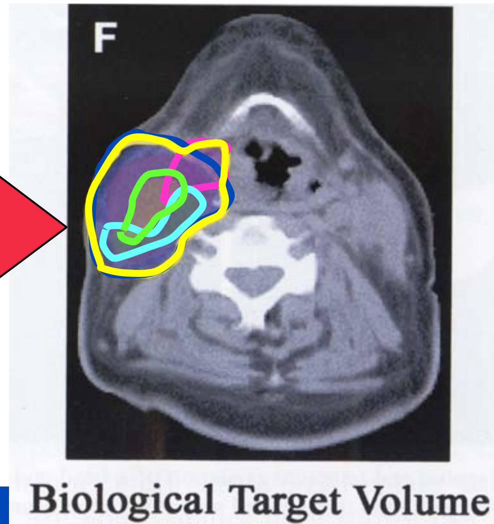

(From
Apisanthanrax,
Rad. Res. 163, 2005)

Molecular Profiling

	Most promising PET- or SPECT-markers[1]:	MRI/ MRS
Hypoxia	^{18}F-FAZA ^{60}Cu-ATSM	BOLD
Cellular Proliferation	^{18}FLT ^{11}C-Met Choline	^{1}H-Cholin-MRS
Apoptosis	Annexin 5	
Angiogenesis	^{18}F-Galacto-RGD	
Receptor status	^{18}F-FES	

1= see Apisarnthanarax 2005

Conclusions

Local tumour control and side effects in radiotherapy strongly depend on our ability to characterize

- Morphology
- Movement
- Molecular Profiling

Conclusions

Local tumour control and side effects in radiotherapy strongly depend on our ability to characterize

- Morphology
- Movement
- Molecular Profiling

While conventional therapy was mainly based on morphology only, we are now starting to include movement and biology, leading to

- Time adapted radiotherapy

and

- Biological adapted radiotherapy

2D/ 3D X-Ray imaging

2D/ 3D X-Ray imaging

- Integrated cone beam imaging/ tomotherapy
- Real-time imaging

2D/ 3D X-Ray imaging

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MRI
fMRI
MRS

2D/ 3D X-Ray imaging

- Integrated cone beam imaging/ tomotherapy
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MRI fMRI MRS

- stronger magnetic fields (3T + 7T)
- Improved resolution
- faster sequences

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SPECT/ PET

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- Integrated cone beam imaging/ tomotherapy
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MRI fMRI MRS

- stronger magnetic fields (3T + 7T)
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SPECT/ PET

- New tracers
  → Molecular Profiling

The future: integration of morphological, functional and biological imaging into radiotherapy

2D/ 3D X-Ray imaging

- Integrated cone beam imaging/ tomotherapy
- Real-time imaging

Radiation Therapy

MRI
fMRI
MRS

- stronger magnetic fields (3T + 7T)
- Improved resolution
- faster sequences

SPECT/ PET

- New tracers
  → Molecular Profiling

2D/ 3D X-Ray
imaging

MRI
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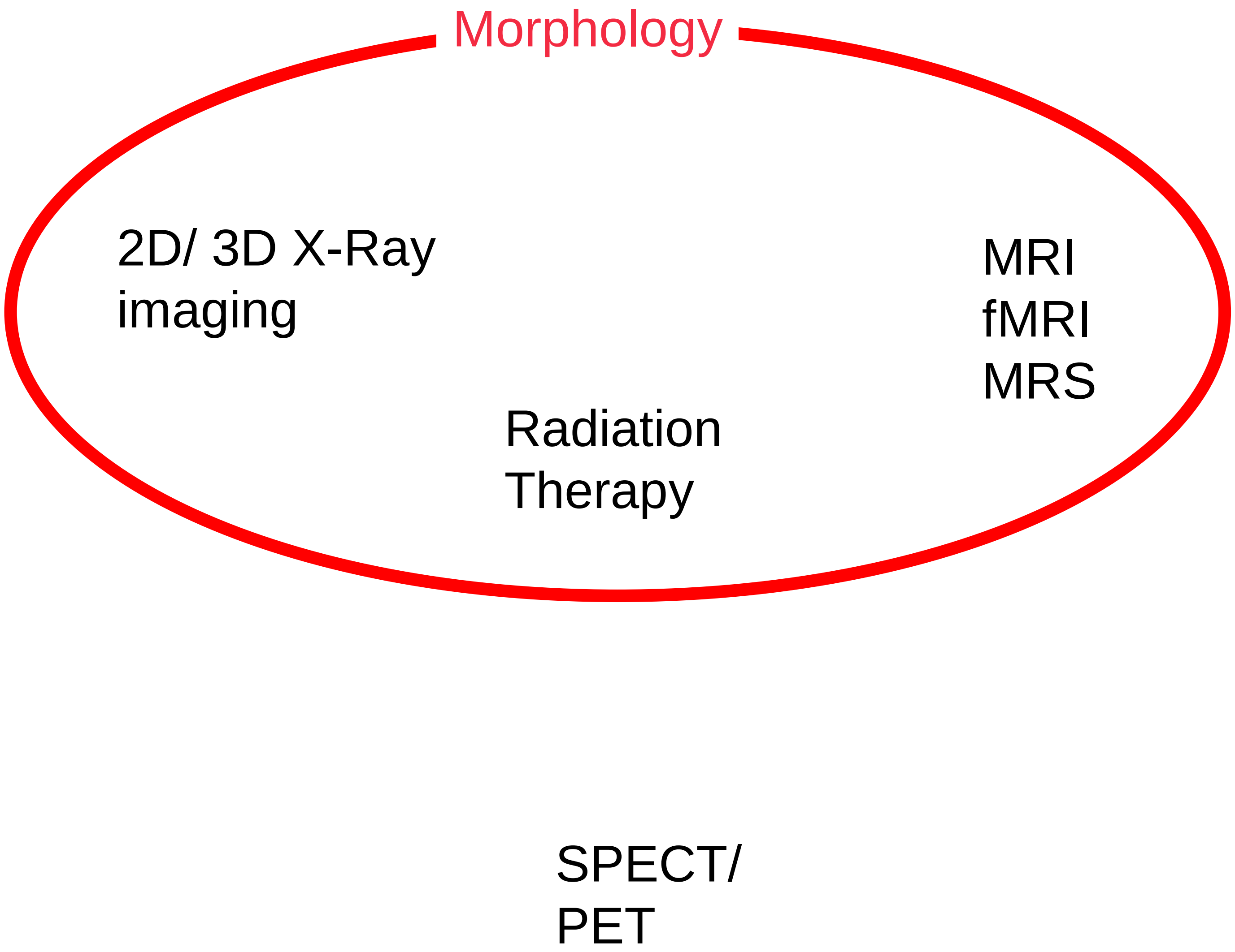
MRS

Radiation
Therapy

SPECT/
PET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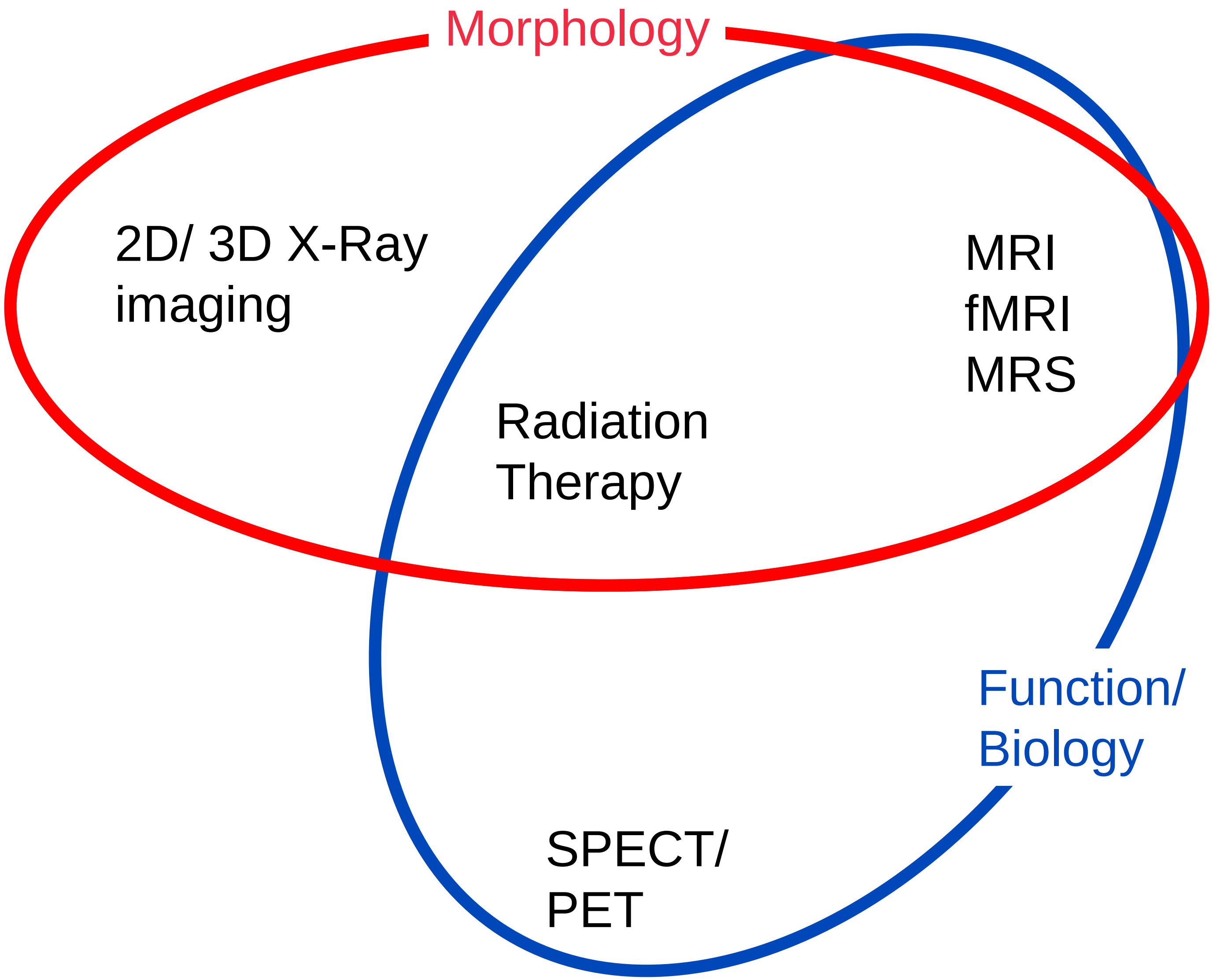
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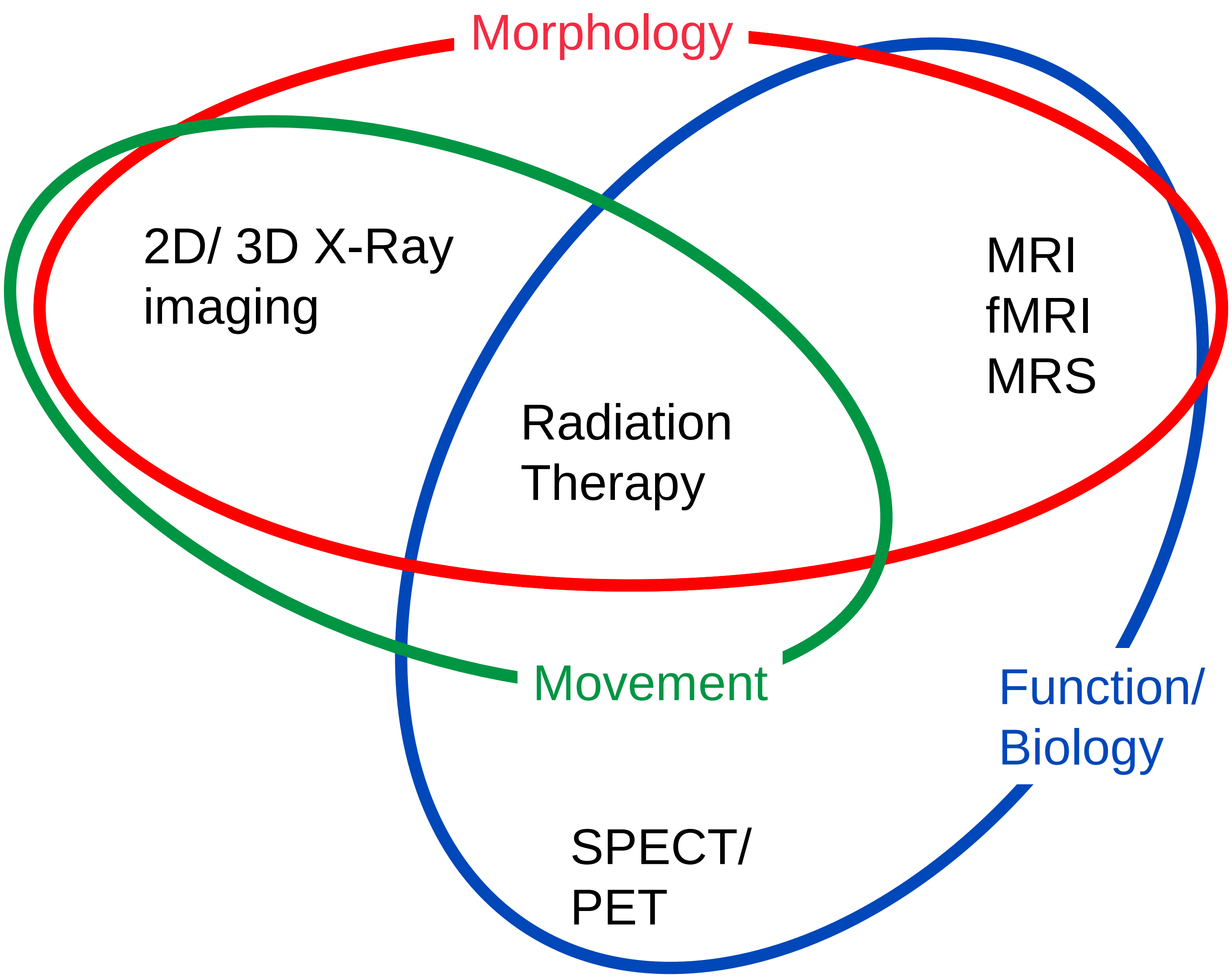
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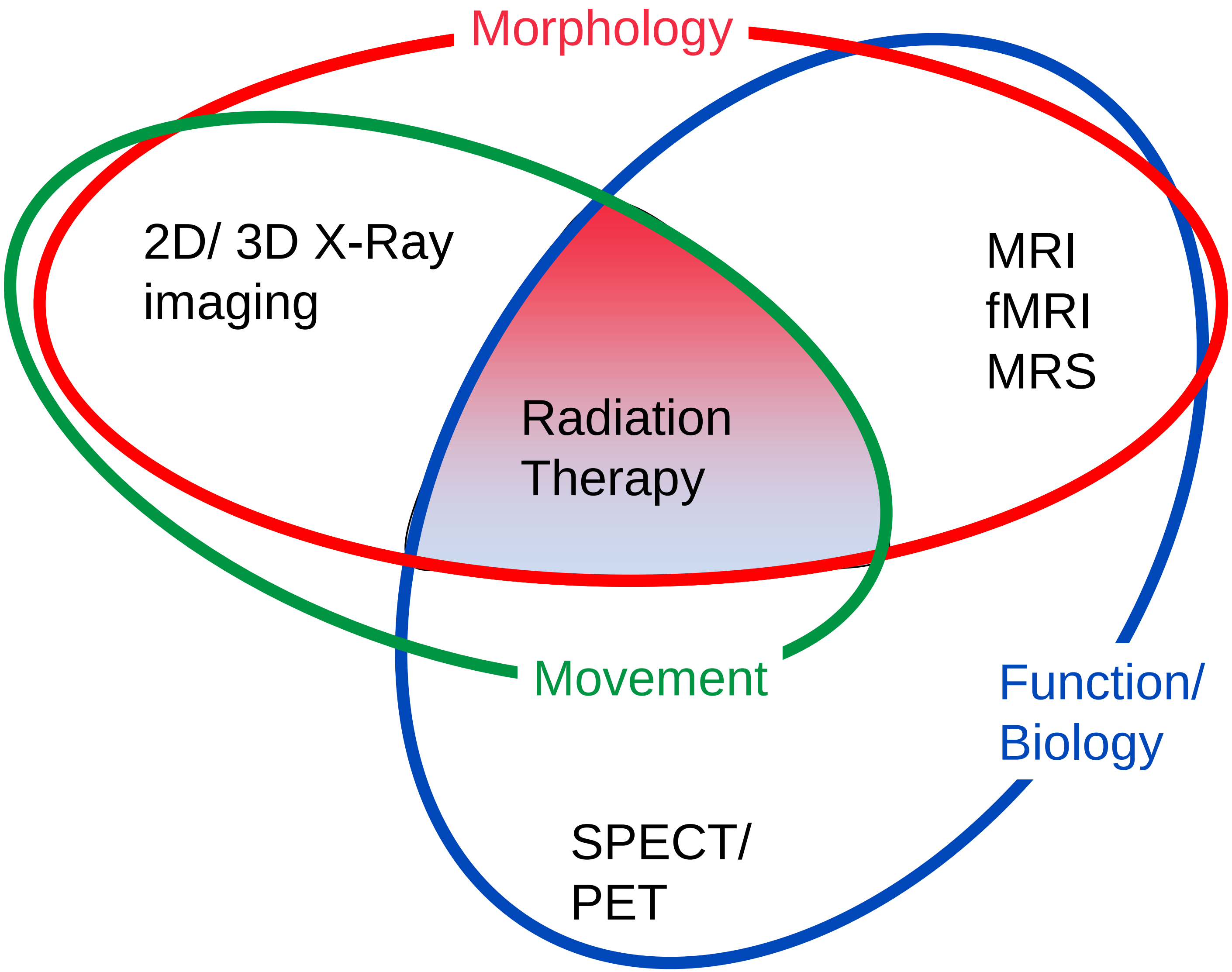
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Integration of morphological,
Functional & biological imaging

The 2nd imaging revolution in Radiation Oncology

Lower side effects

Improved local
tumour control