iridium kankernetwerk

AZ Klina
Brasschaat

AZ Monica
Antwerpen – Deurne

AZ Nikolaas
Sint-Niklaas,
Partner AZ Lokeren

AZ Sint-Jozef
Malle

GZA Ziekenhuizen
Antwerpen – Mortsel – Wilrijk

UZA
Edegem

ZNA
Antwerpen - Merksem

Sparen van gezonde weefsels d.m.v. innovatieve radiotherapie

Piet Dirix MD, PhD

Radiotherapie-Oncologie

Iridium Kankernetwerk

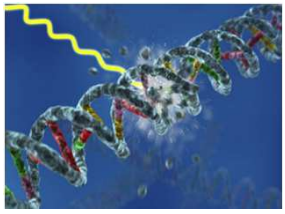
www.iridiumkankernetwerk.be

Universiteit Antwerpen

Gray = physical unit of radiation

- Dose = absorbed E/mass
- Gray = unit of absorbed E (Joule/kg)
- 1 Gy = 2 x 10^5 ionization events/cell

  (1% in DNA)



repair

incorrect repair

no repair

cell survival

mutation

cell death

cancer

iridium kankernetwerk

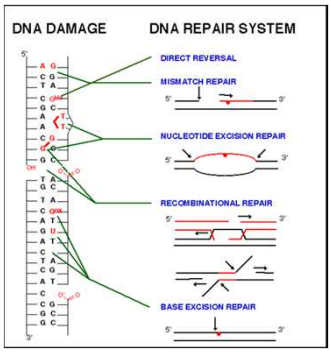
Fractionation

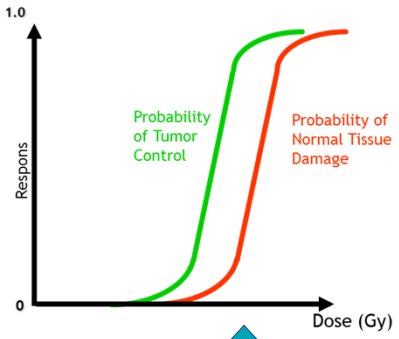
3 x 3.3 Gy

5 x 2 Gy

iridium kankernetwerk

The biological basis of fractionation





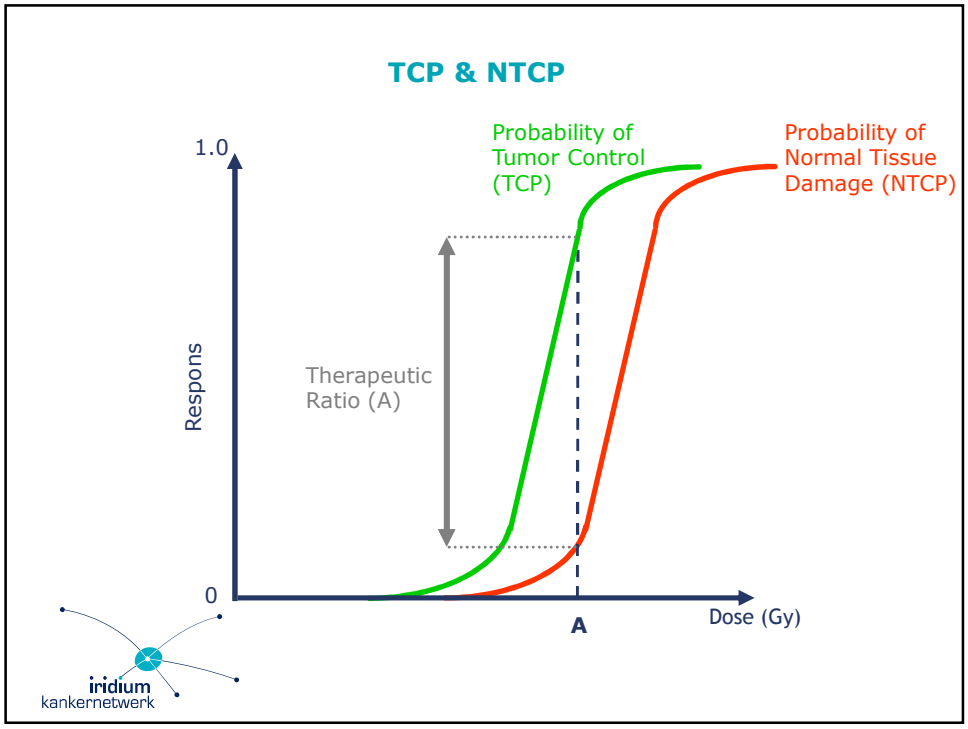
Difference of DNA Repair
Tumour Cells < Healthy Tissue

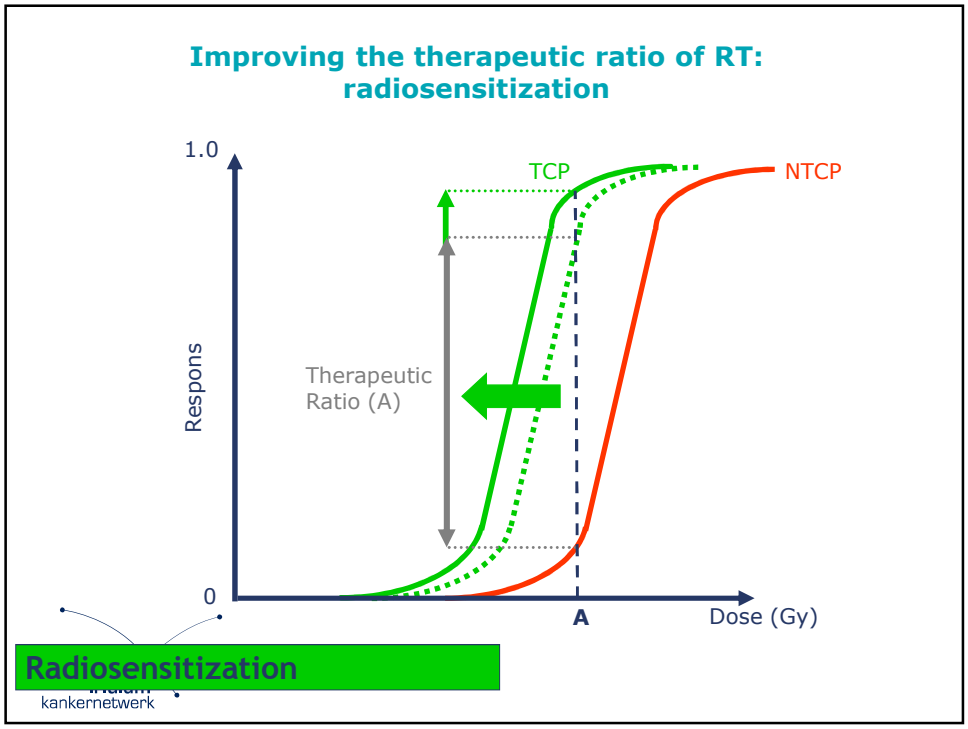
Dose Dose Dose Dose Dose Dose Dose Dose Dose Dose Dose

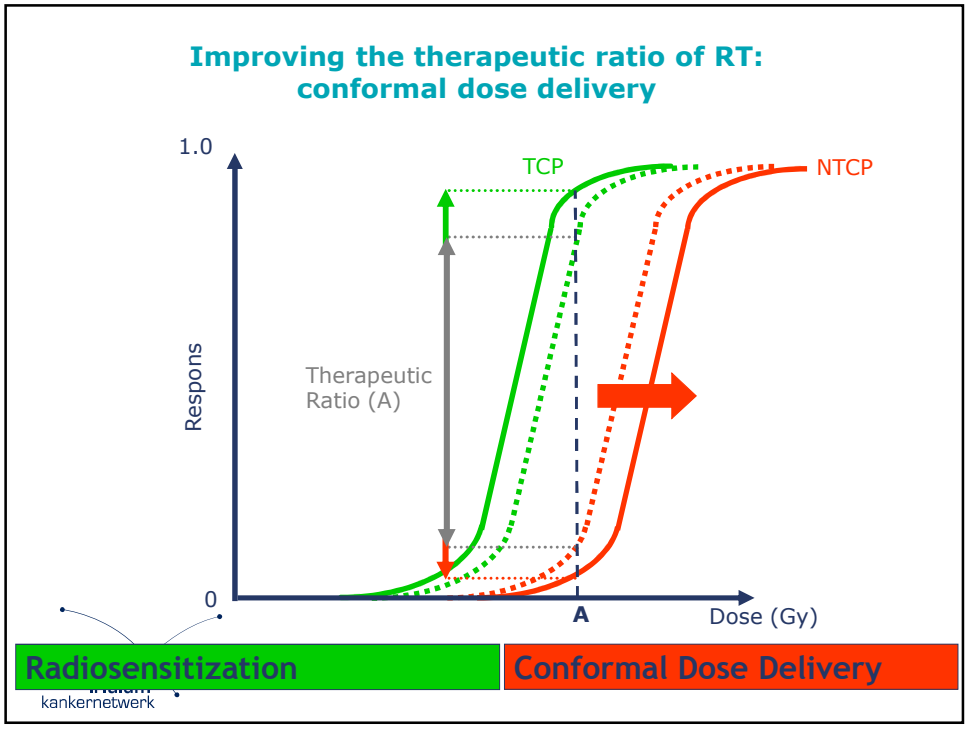
"Fractionation"

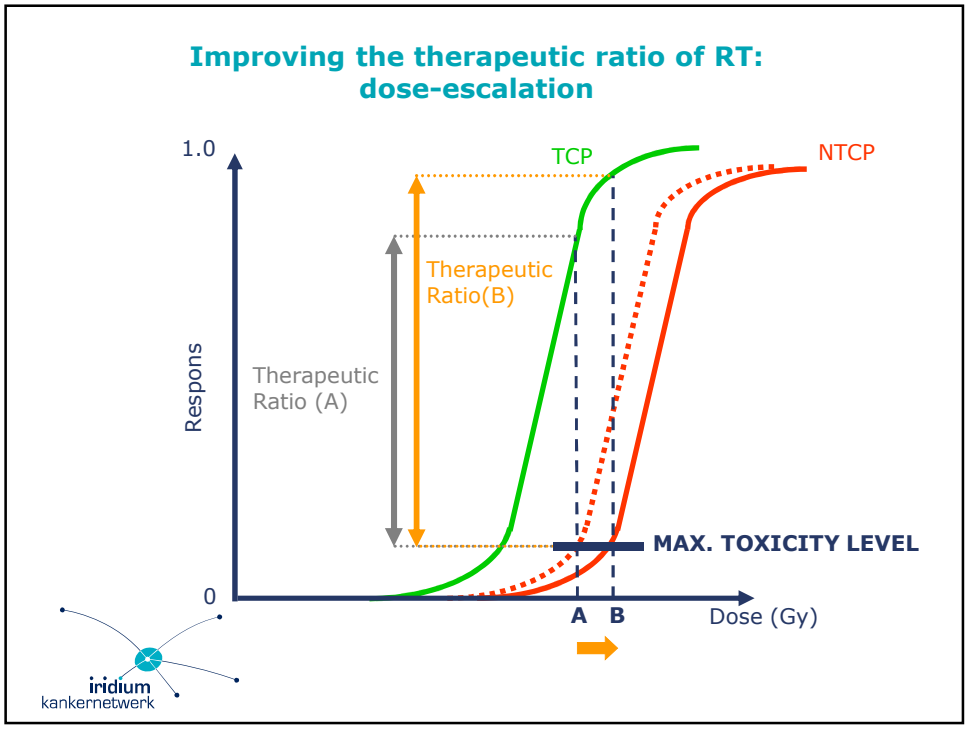
Dose

iridium kankernetwerk


TCP & NTCP
Probability of Tumor Control (TCP)
Probability of Normal Tissue Damage (NTCP)
1.0
Respons
Therapeutic Ratio (A)
0
A
Dose (Gy)
iridium
kankernetwerk

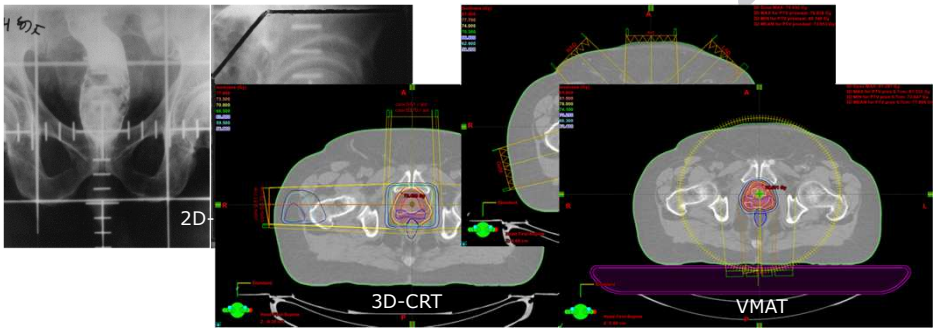

Improving the therapeutic ratio of RT: radiosensitization
1.0
TCP
NTCP
Respons
Therapeutic Ratio (A)
0
A
Dose (Gy)
Radiosensitization
kankernetwerk


Improving the therapeutic ratio of RT:
conformal dose delivery
1.0
0
Respons
TCP
NTCP
Therapeutic
Ratio (A)
A
Dose (Gy)
Radiosensitization
Conformal Dose Delivery
kankernetwerk


Improving the therapeutic ratio of RT:
dose-escalation
1.0
0
Respons
TCP
NTCP
Therapeutic
Ratio(B)
Therapeutic
Ratio (A)
MAX. TOXICITY LEVEL
A
B
Dose (Gy)
iridium
kankernetwerk

Evolution of radiotherapy techniques

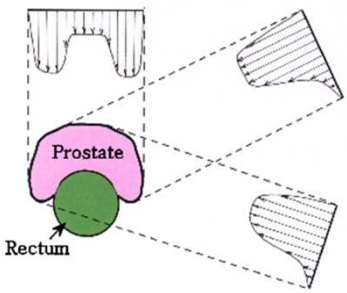
2D-RT 1990 3D-CRT 2000 IMRT 2010 VMAT

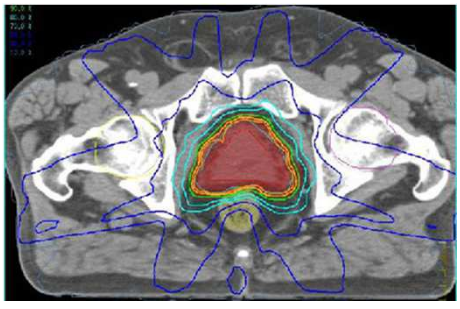


Radiorectitis = dose-limiting toxicity (DLT)

iridium kankernetwerk

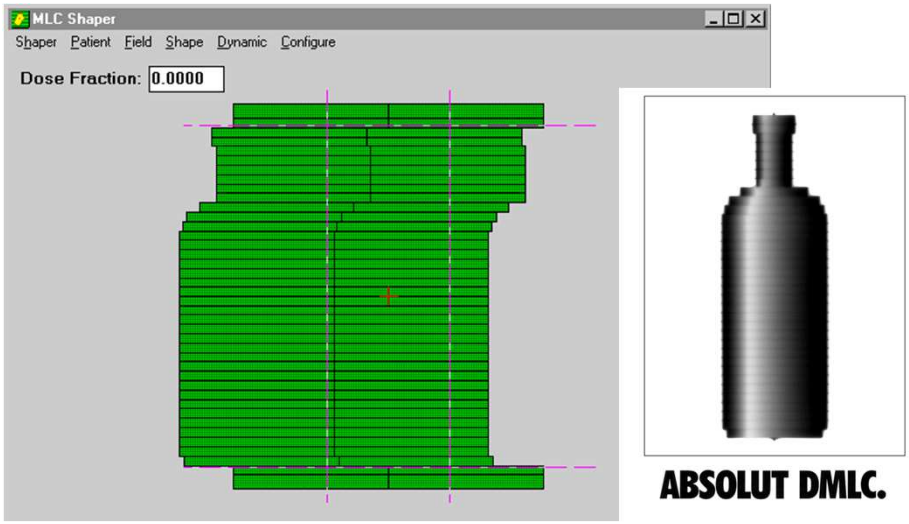
Intensity-modulated radiotherapy (IMRT)





iridium kankernetwerk

Multileaf collimator (MLC)



iridium kankernetwerk

SEER database

Table 3. Unadjusted and Propensity-Model Adjusted Outcomes for IMRT vs CRT

Outcome per 100 Person-Years	Unadjusted: CRT (n = 6310) Total Events	100 Person-Years	Rate	IMRT (n = 6666) Total Events	100 Person-Years	Rate	IMRT vs CRT, Rate Ratio (95% CI)	Adjusted[a]: CRT (n = 6478) Total Events	100 Person-Years	Rate	IMRT (n = 6438) Total Events	100 Person-Years	Rate	IMRT vs CRT, Rate Ratio (95% CI)
Gastrointestinal events														
Procedures (including colonoscopy)	3187	195	16.3	2940	167	17.6	1.08 (1.03-1.13)	2989	180	16.6	3011	177	17.0	1.02 (0.97-1.07)
Diagnoses	2946	212	13.9	2450	182	13.5	0.97 (0.92-1.02)	2828	192	14.7	2594	194	13.4	0.91 (0.86-0.96)
Urinary nonincontinence events														
Procedures	564	293	1.9	439	234	1.9	0.98 (0.86-1.11)	493	260	1.9	483	257	1.9	0.99 (0.87-1.12)
Diagnoses	2003	248	8.1	1747	199	8.8	1.09 (1.02-1.16)	1941	220	8.8	1869	214	8.8	0.99 (0.93-1.06)
Urinary incontinence events														
Procedures	1904	246	7.7	1854	194	9.5	1.23 (1.16-1.32)	1867	219	8.5	1888	211	8.9	1.05 (0.98-1.12)
Diagnoses	970	283	3.4	785	226	3.5	1.01 (0.92-1.11)	917	251	3.7	858	249	3.5	0.94 (0.86-1.04)
Erectile dysfunction events														
Procedures	202	303	0.7	200	240	0.8	1.25 (1.03-1.52)	224	268	0.8	200	265	0.8	0.90 (0.75-1.09)
Diagnoses	1186	265	4.5	1342	208	6.5	1.44 (1.33-1.56)	1239	235	5.3	1342	228	5.9	1.12 (1.03-1.20)
Hip fracture	301	302	1.0	186	240	0.8	0.78 (0.65-0.93)	272	267	1.0	209	265	0.8	0.78 (0.65-0.93)
Additional cancer therapy	896	302	3.0	575	249	2.3	0.78 (0.70-0.87)	839	270	3.1	677	270	2.5	0.81 (0.73-0.89)

Abbreviations: CRT, conformal radiation therapy; IMRT, intensity-modulated radiation therapy.
[a]Rates shown are adjusted for the variables presented in Tables 1 and 2, using propensity scores implemented by inverse probability of treatment weighting.

iridium kankernetwerk

Sheets N.C. et al. JAMA 2012.

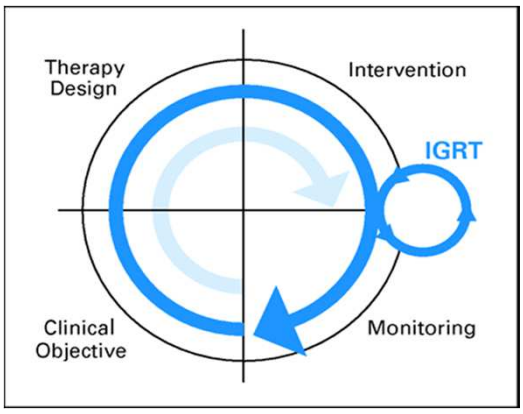
VMAT

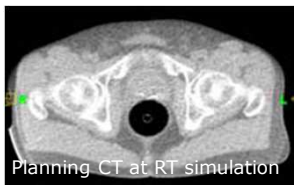
Advantages over "conventional" IMRT:

- **Fast (< 2 minutes):**
  - Limits intra-fraction motion
  - Increases patient comfort
  - Reduces waiting lists
  - Probable radiobiological advantage
- **Highly conformal:**
  modulate at every angle
  - Gantry speed
  - MLC aperture shape
  - Dose rate

iridium kankernetwerk

Image-guided radiotherapie (IGRT)




Planning CT at RT simulation

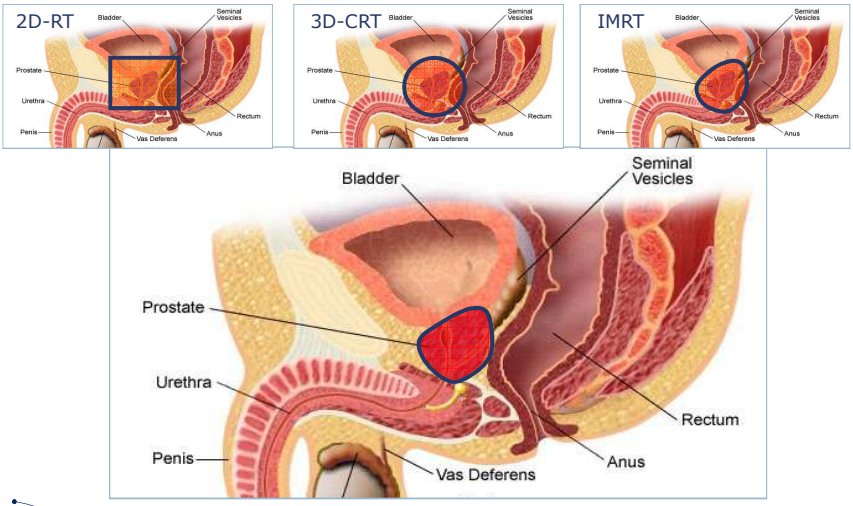

CT at RT delivery

IGRT = making sure that treatment is delivered as planned

iridium kankernetwerk

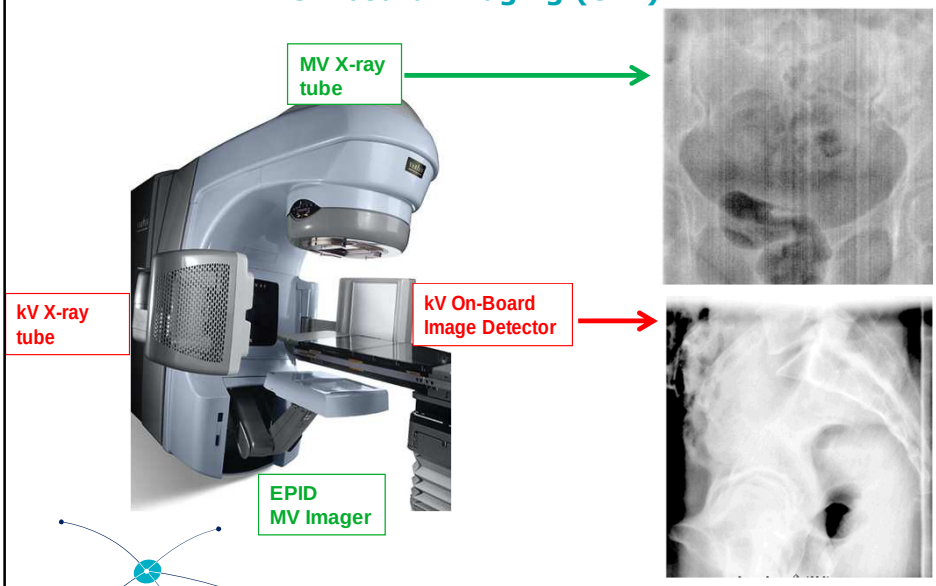
Dawson J. et al. J Clin Oncol 2007.

IGRT for prostate cancer



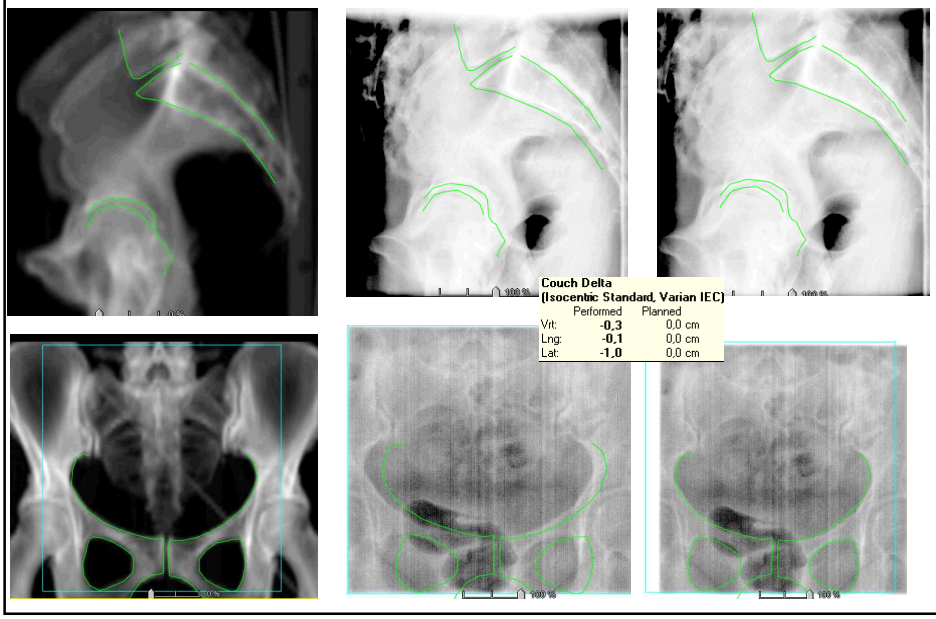
iridium kankernetwerk

On-board Imaging (OBI)



iridium kankernetwerk

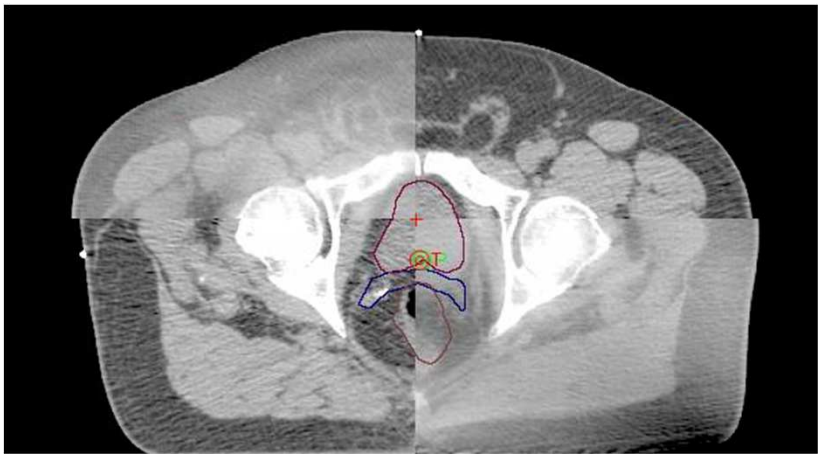
kV-MV "matching" on bony anatomy



kV-MV "matching" on fiducial markers

iridium
kankernetwerk

CB-CT "matching" on soft tissue



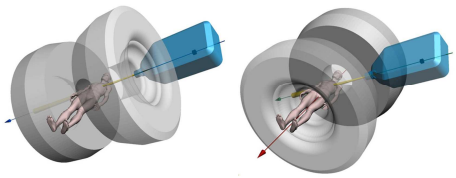
iridium kankernetwerk

MR "matching" on MR-Linac

MRIdian (ViewRay)

Unity (Elekta-Philips)

Australian MR-Linac program



University of Alberta

iridium kankernetwerk

Dirix P. et al. Semin Radiat Oncol 2014.

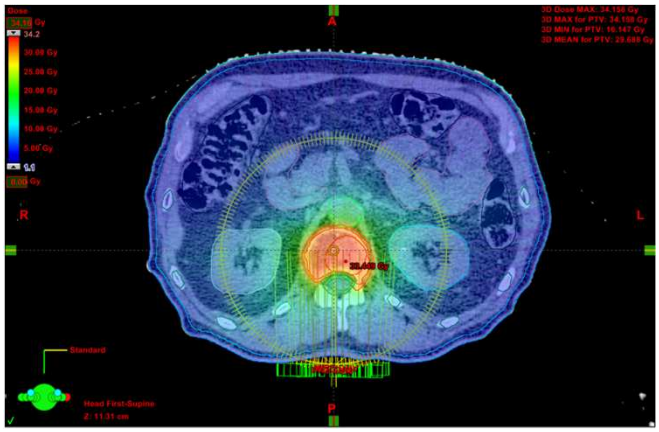
MR-LINACS will allow for true soft tissue matching

Linac – Cone-beam CT		MR-LINAC
		
✖	Eliminate X-ray radiation	✔
✖	Don't use registration markers	✔
✖	Differentiate between soft tissues and tumor	✔
✖	Ability to locate, target and track the tumor directly	✔

iridium kankernetwerk

Dirix P. et al. Semin Radiat Oncol 2014.

Ultimate combination of IMRT and IGRT: SABR



1. GTV delineated on MRI and/or PET.
2. No or limited CTV.
3. PTV margins < 0,5 cm.
4. Good quality daily IGRT is essential.
5. Extremely hypofractionated.

SABR = stereotactic ablative body radiotherapy

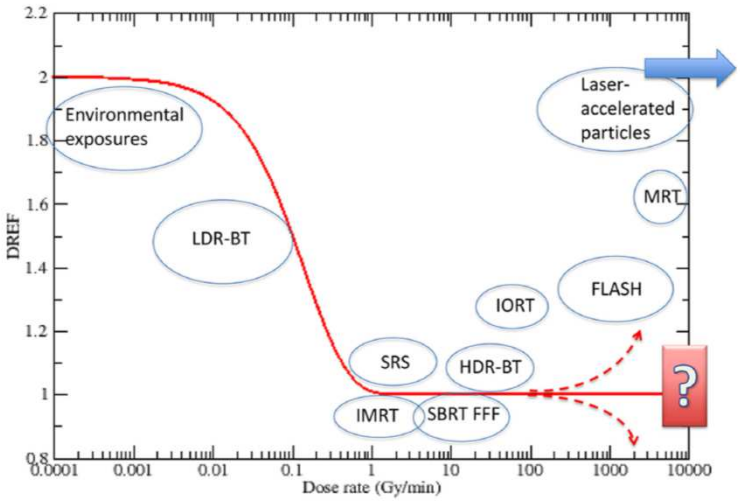
iridium kankernetwerk

Hypofractionation

Target volume	Previous fractionation	Current fractionation	SABR alternative
Brain tumors	30x 2,0 Gy	15x 2,67 Gy	SRS
Breast cancer	25x 2,0 Gy	15x 2,67 Gy	APBI
Lung cancer	30-33x 2,0 Gy	16-20x 2,75 Gy	Lung SBRT
Rectal cancer	25x 1,8 Gy	5x 5,0 Gy	-
Prostate cancer	37-40x 2,0 Gy	20x 3,0 Gy	5x 7,0 Gy
Bladder cancer	33x 2,0 Gy	15x 2,75 Gy	-
Bone mets	10x 3,0 Gy	1x 8,0 Gy	1x 16,0 Gy
…			

iridium kankernetwerk

Cured in a FLASH?



iridium kankernetwerk

Durante M. et al. Br J Radiol 2018.

Conclusions

- Radiation delivery already has **potential ≤ 1 mm accuracy**.
- From a **physics** point of view, the greatest improvements can be expected from:
  - **Imaging**, both before and during RT, allowing us to see and therefore hit the target more precisely.
  - Experiments in **ultra-high dose rate (FLASH)** radiotherapy.
- From a **biology** point of view, we should probably invest in:
  - More precise **radiosensitization** (e.g. TGF-β).
  - Individualized **dose prescription**.

iridium
kankernetwerk