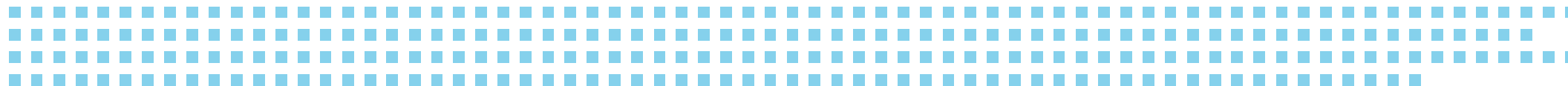


INNOVATIE IN DE RADIOThERAPIE

nieuwste technieken en ontwikkeling in de behandeling van cervixcarcinoom

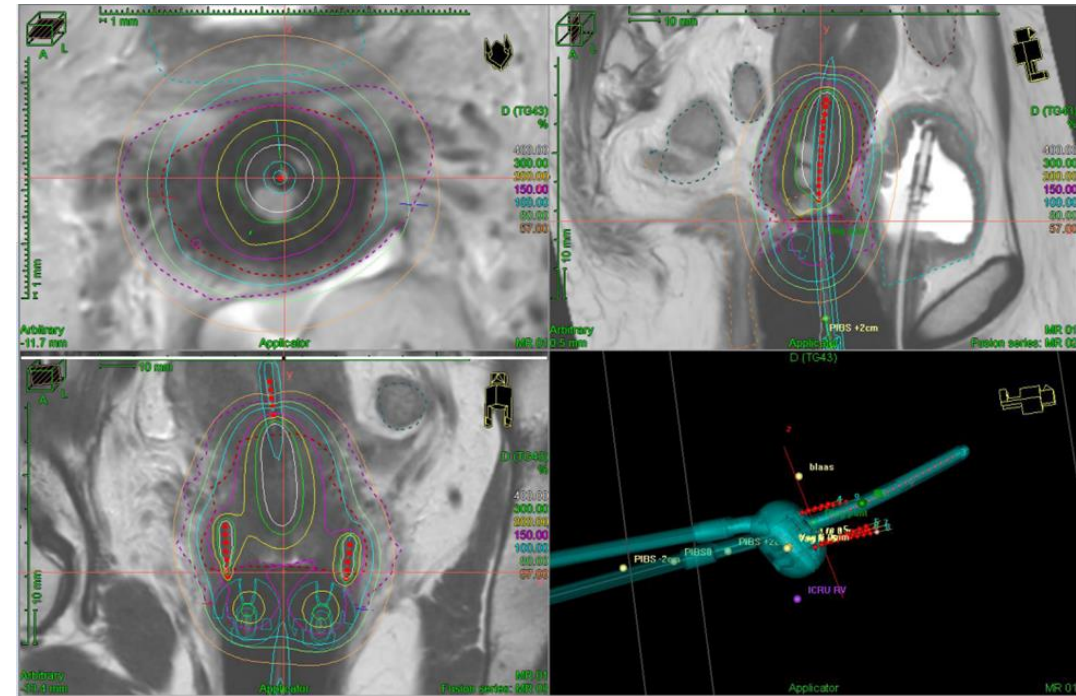
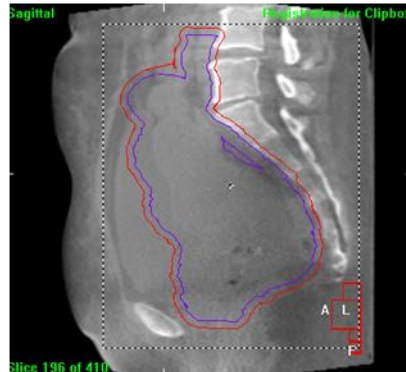
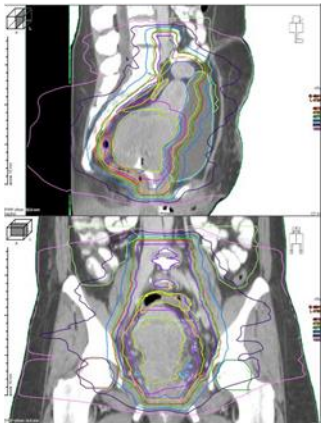
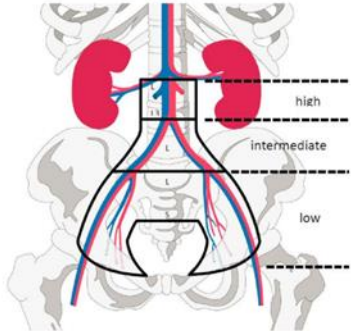
Henrike Westerveld, radiotherapeut EMC, DGOG symposium 19.01.2023



CURRENT STANDARD OF CARE

Primary chemoradiation in patients with FIGO stage IB3 and higher

- EBRT (25 fractions, 45/55-57.5Gy) with weekly cisplatin 40mg/m² (or DHT)
- Image-guided adaptive brachytherapy boost (D90 HRCTV 90-95 Gy)



GEC-ESTRO GYN WG & EMBRACE

Clinical and Translational Radiation Oncology 9 (2018) 48–60



Contents lists available at ScienceDirect

Clinical and Translational Radiation Oncology

journal homepage: www.elsevier.com/locate/ctro



Review Article

The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies

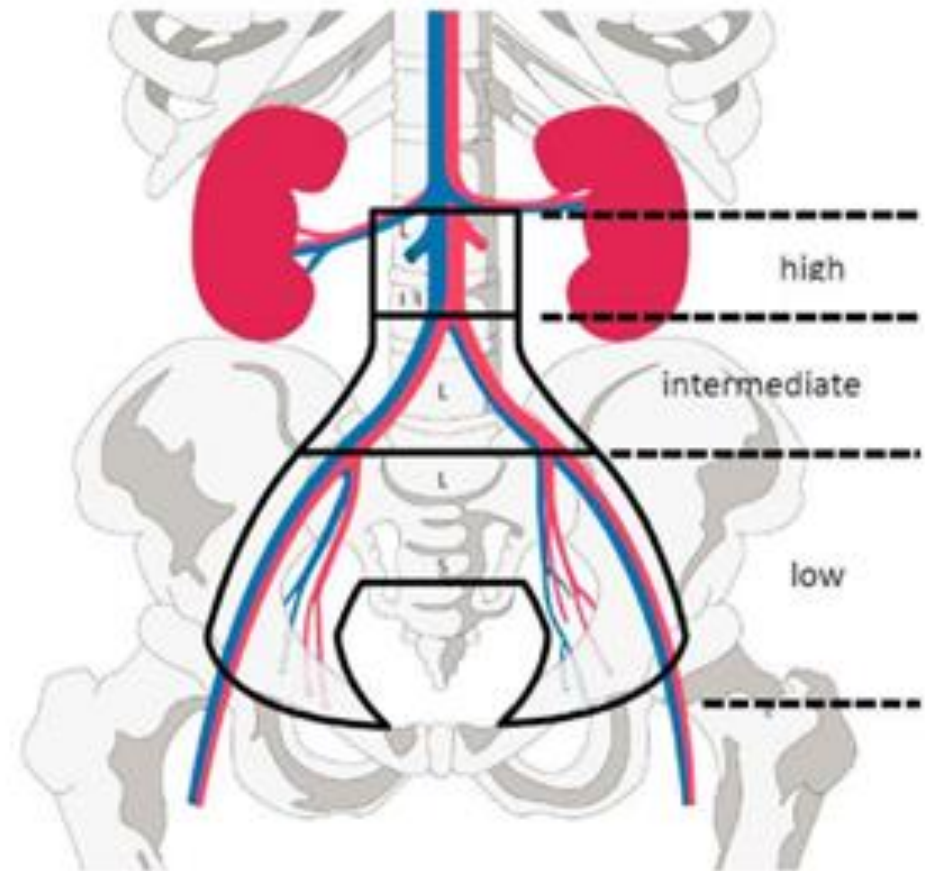


Richard Pötter^{a,1}, Kari Tanderup^{b,1,*}, Christian Kirisits^a, Astrid de Leeuw^c, Kathrin Kirchheiner^a, Remi Nout^d, Li Tee Tan^e, Christine Haie-Meder^f, Umesh Mahantshetty^g, Barbara Segedin^h, Peter Hoskinⁱ, Kjersti Bruheim^j, Bhavana Rai^k, Fleur Huang^l, Erik Van Limbergen^m, Max Schmid^a, Nicole Nesvacil^a, Alina Sturdza^a, Lars Fokdal^b, Nina Boje Kibsgaard Jensen^b, Dietmar Georg^a, Marianne Assenholt^b, Yvette Seppenwoolde^a, Christel Nomden^c, Israel Fortin^{a,o}, Supriya Chopra^g, Uulke van der Heideⁿ, Tamara Rumpold^a, Jacob Christian Lindegaard^b, Ina Jürgenliemk-Schulz^c, the EMBRACE Collaborative Group²

CURRENT STANDARD OF CARE

External beam radiotherapy (EBRT)

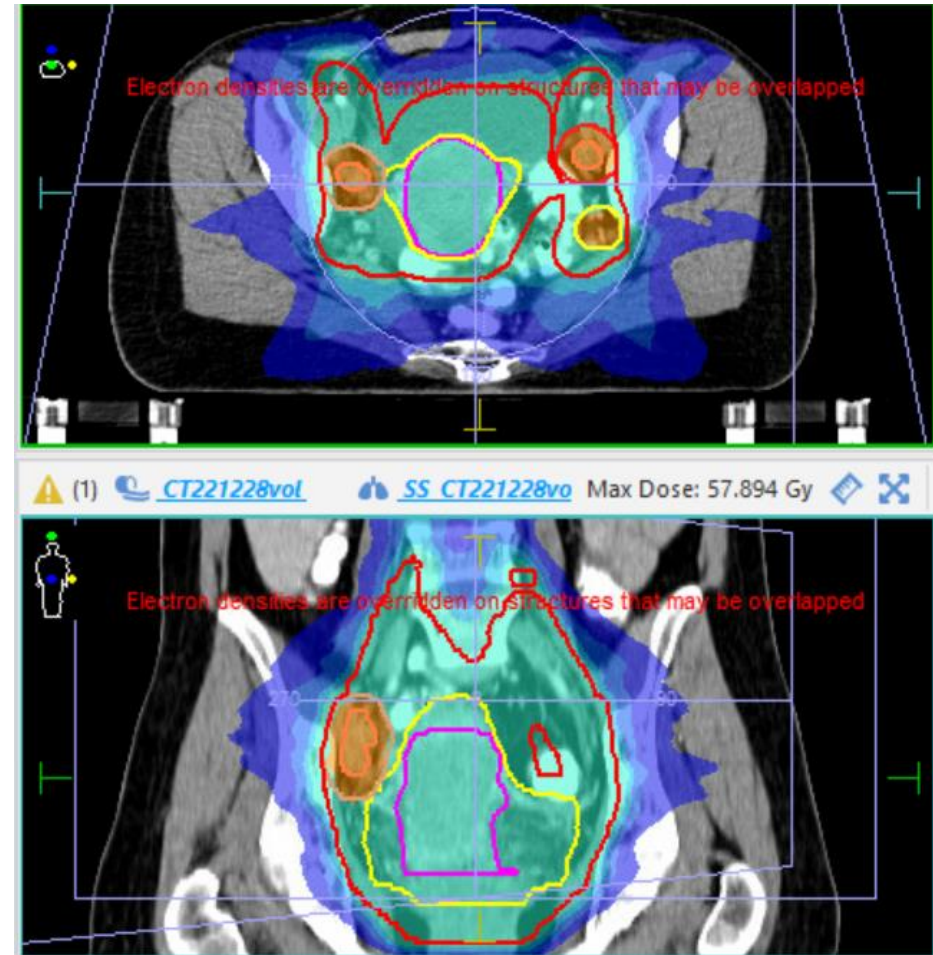
- Risk stratified radiation field



CURRENT STANDARD OF CARE

External beam radiotherapy (EBRT)

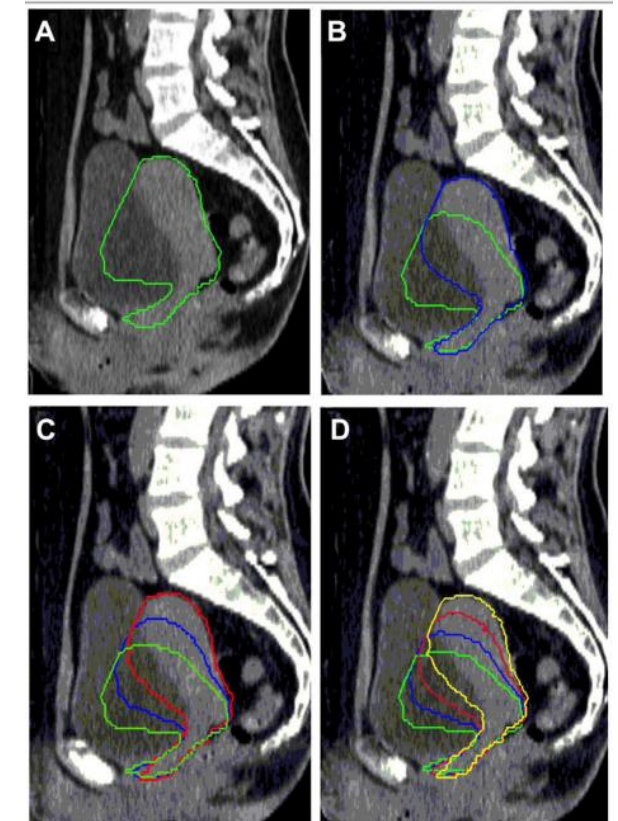
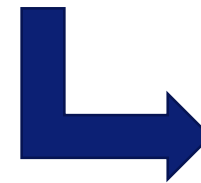
- Risk stratified radiation field
- Standard fractionation schedule: 25 fractions with a simultaneous integrated boost (SIB) in cases of N+ disease



CURRENT STANDARD OF CARE

External beam radiotherapy (EBRT)

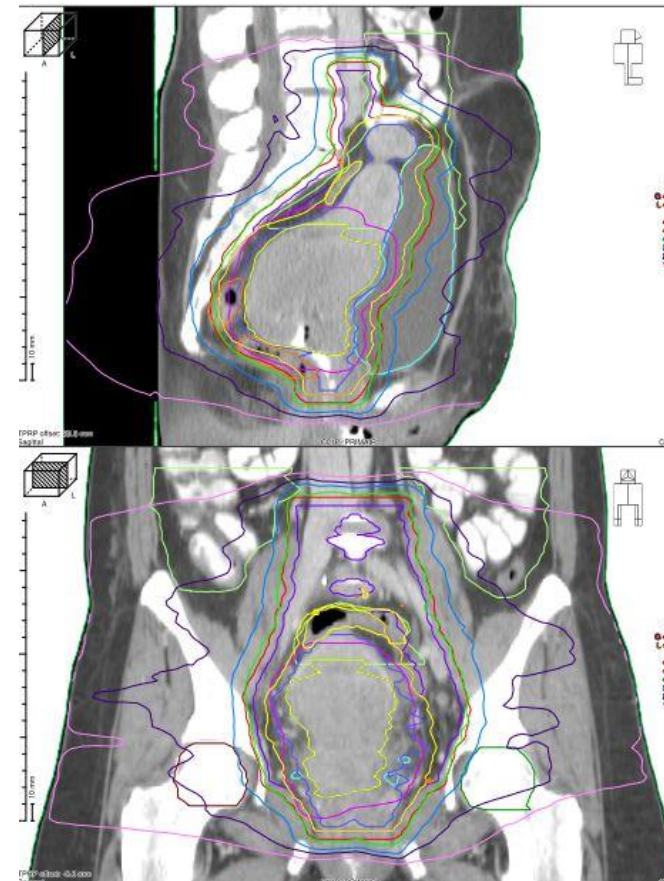
- Risk stratified radiation field
- Standard fractionation schedule: 25 fractions with a simultaneous integrated boost (SIB) in cases of N+ disease
- Library of plans



CURRENT STANDARD OF CARE

External beam radiotherapy (EBRT)

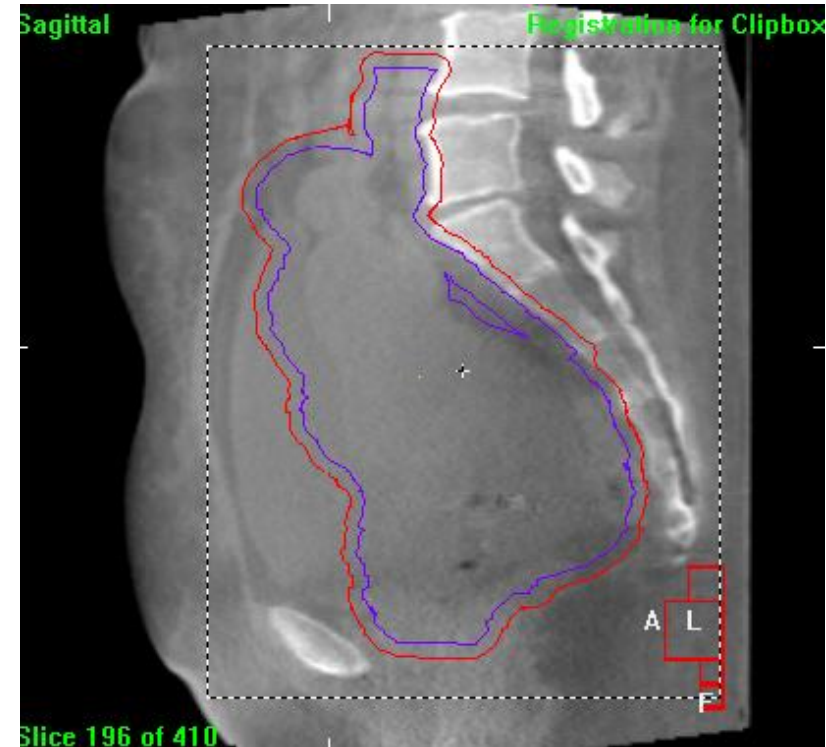
- Risk stratified radiation field
- Standard fractionation schedule: 25 fractions with a simultaneous integrated boost (SIB) in cases of N+ disease
- Library of plans
- VMAT/IMRT



CURRENT STANDARD OF CARE

External beam radiotherapy (EBRT)

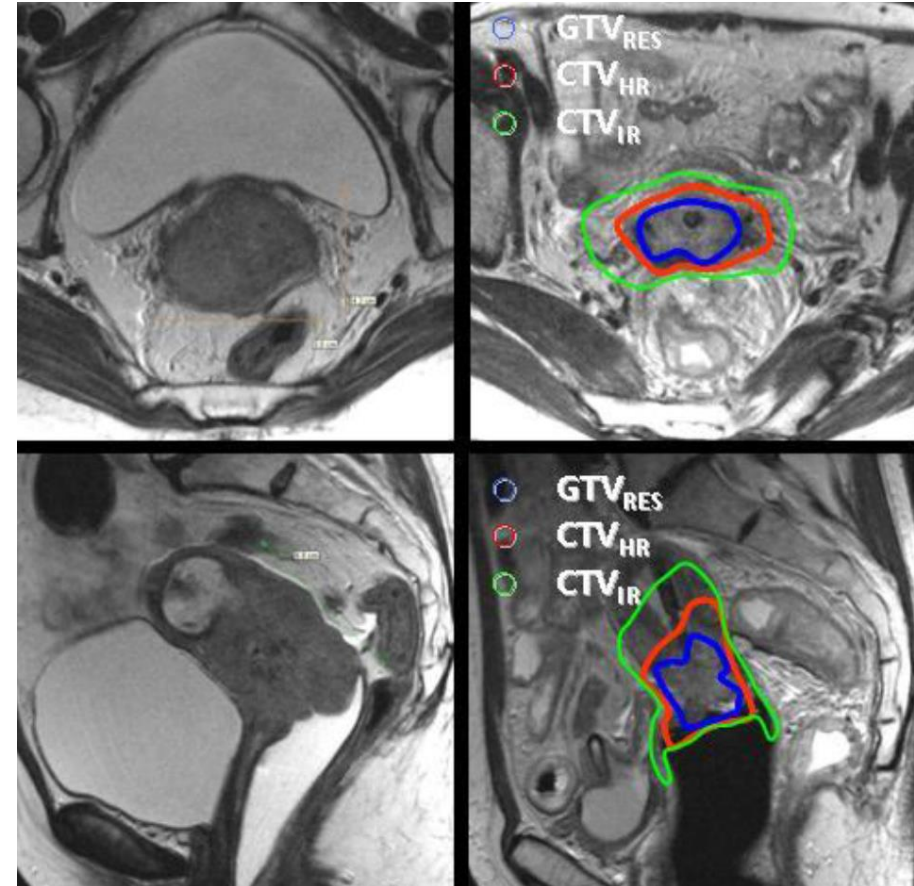
- Risk stratified radiation field
- Standard fractionation schedule: 25 fractions with a simultaneous integrated boost (SIB) in cases of N+ disease
- Library of plans
- VMAT/IMRT
- Daily positioning verification



CURRENT STANDARD OF CARE

MRI-guided adaptive brachytherapy (IGABT)

- MRI guided for better visualization of the clinical target volume



CURRENT STANDARD OF CARE

MRI-guided adaptive brachytherapy (IGABT)

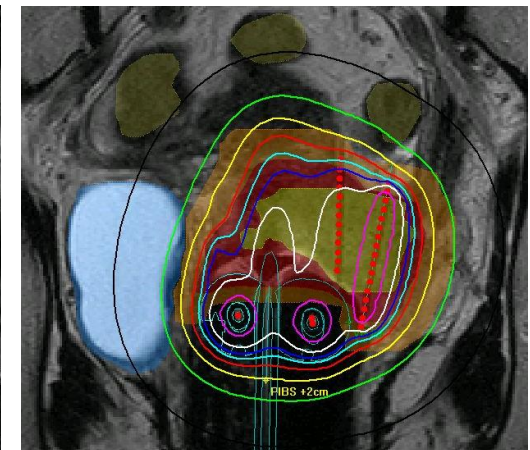
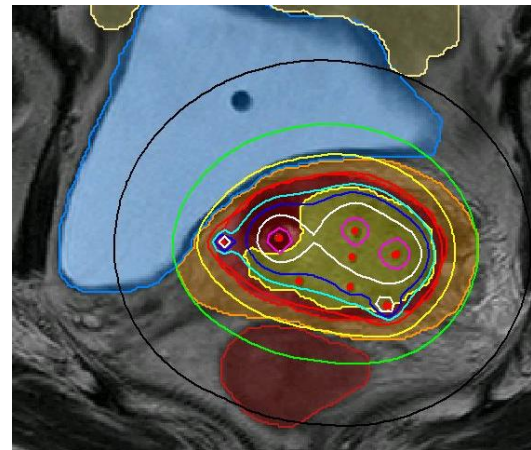
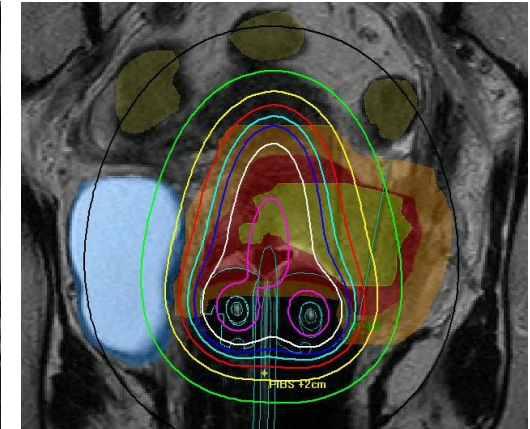
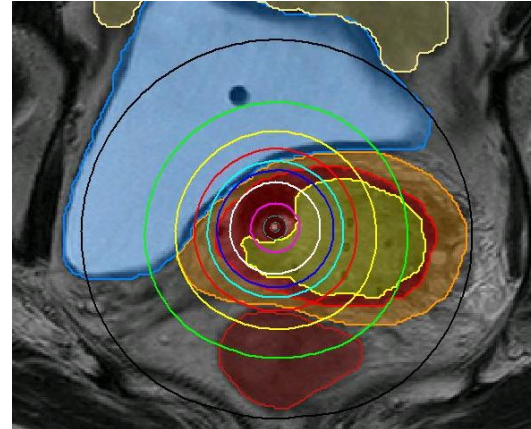
- MRI guided for better visualization of the clinical target volume
- MRI compatible intracavitary & interstitial applicators



CURRENT STANDARD OF CARE

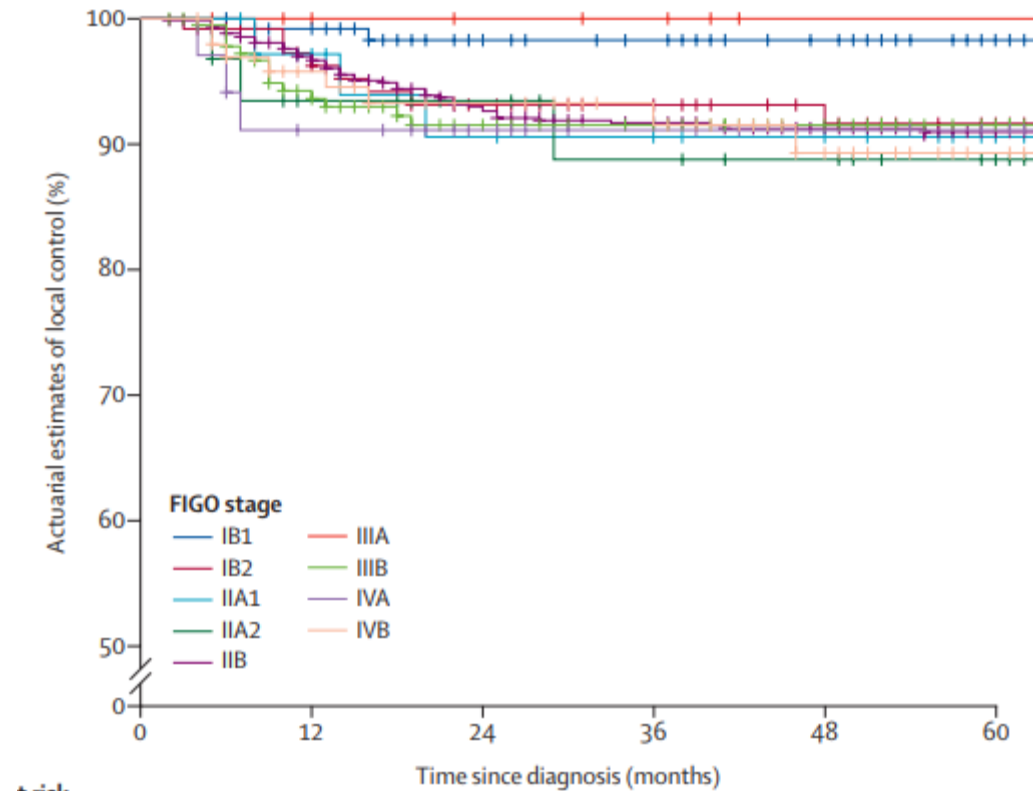
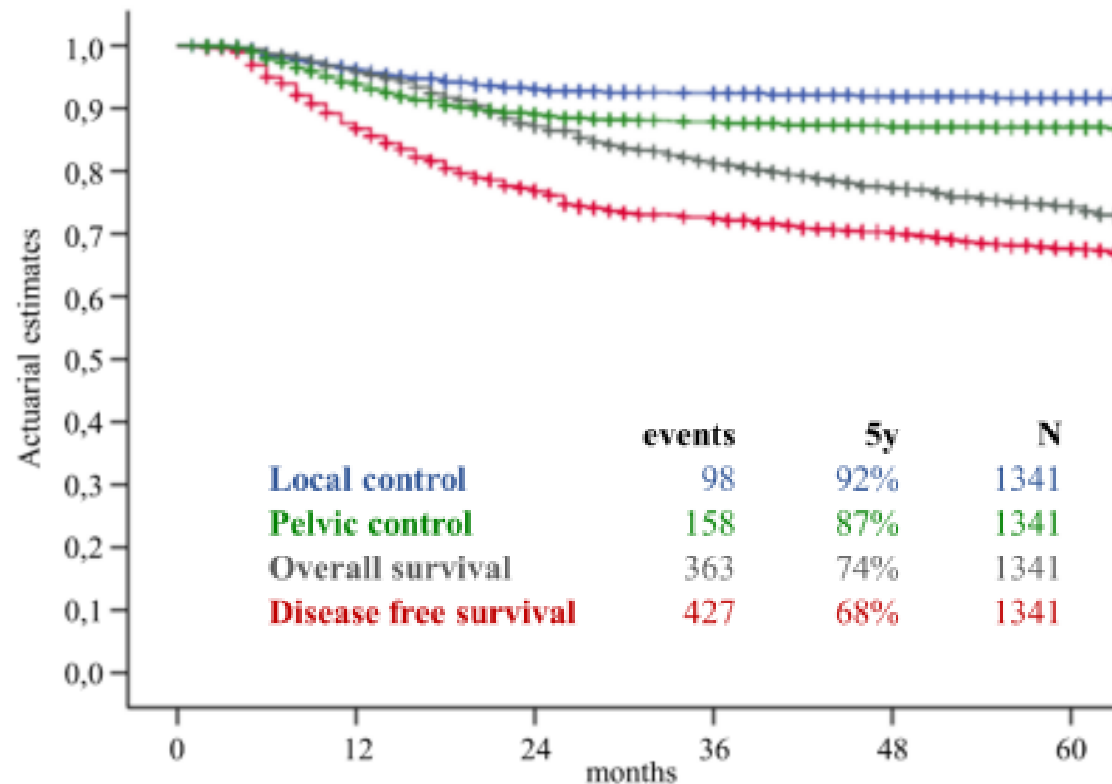
MRI-guided adaptive brachytherapy (IGABT)

- MRI guided for better visualization of the clinical target volume
- MRI compatible intracavitary & interstitial applicators
- Highly conformal planning leading to:
 - Better coverage of the tumour
 - Better sparing of OARs



25%
50%
75%
100%
125%
150%
200%
400%

EMBRACE-I MRI guided adaptive BT

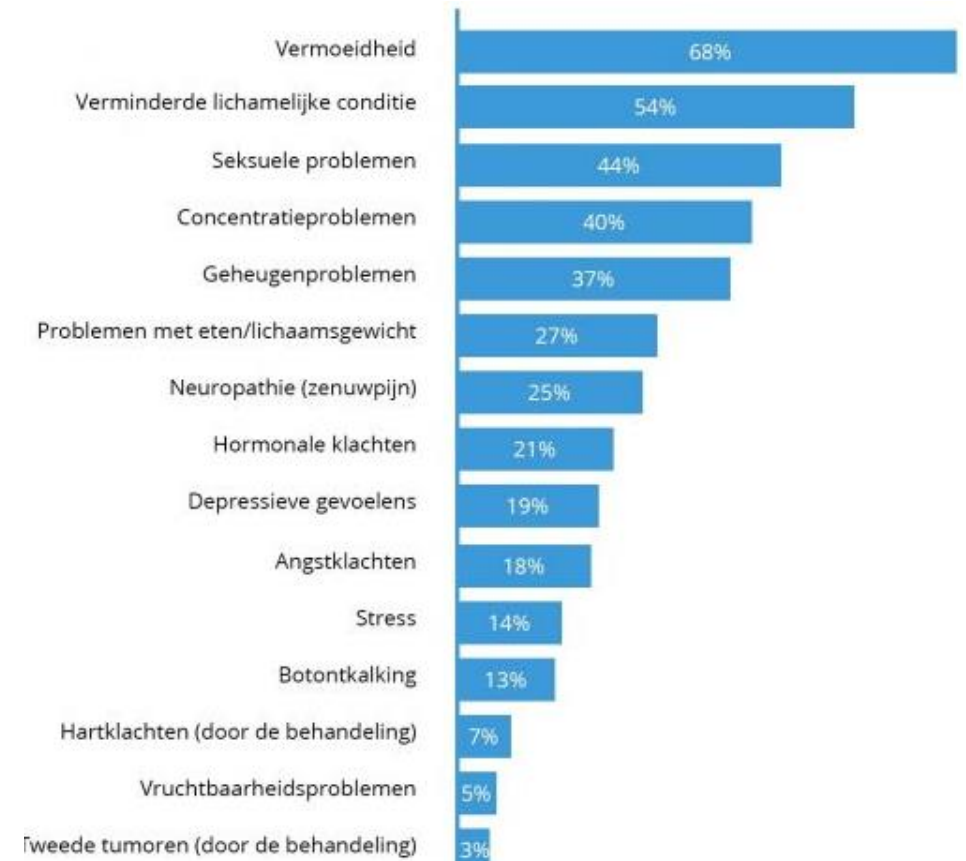


- Actuarial 5-year \geq G3 morbidity: GU: 6.8%; GI: 8.5%; vaginal 5.7%; and fistulae 3.2%
- Any \geq G3 morbidity actuarial 5-year: 26%

BUT WE AREN'T THERE YET...

Quality of life after treatment for cervical cancer

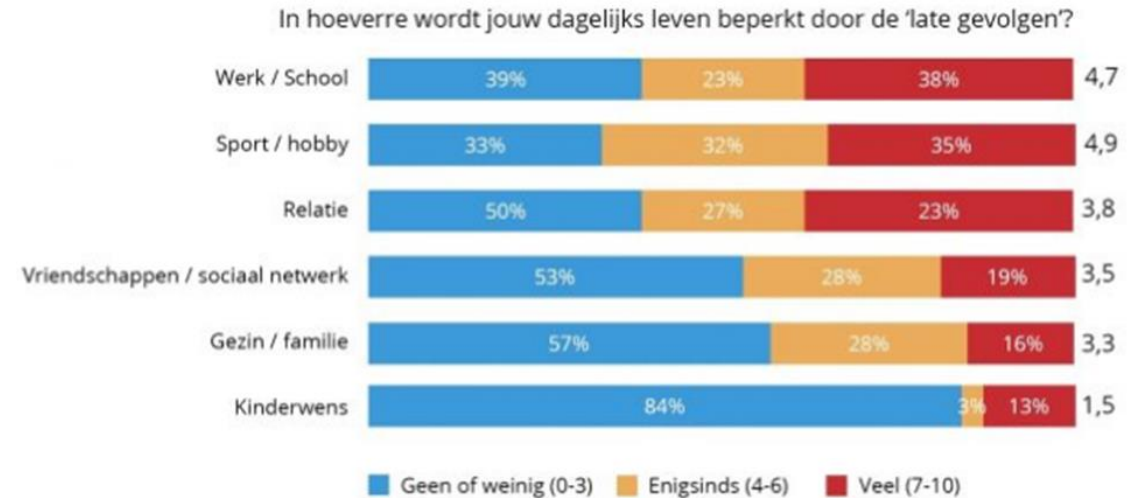
- Many women have and hold complaints after gynaecological cancer treatment



BUT WE AREN'T THERE YET...

Quality of life after treatment for cervical cancer

- Many women have and hold complaints after gynaecological cancer treatment
- Complaints are on the physical, mental and cognitive domains, and interfere with patients' daily functioning, and have a negative impact on quality of life and social wellbeing/role



BUT WE AREN'T THERE YET...

Quality of life after treatment for cervical cancer

- Many women have and hold complaints after gynaecological cancer treatment
- Complaints are on the physical, mental and cognitive domains, and interfere with patients' daily functioning, and have a negative impact on quality of life and social wellbeing/role
- According to the patients, the physician doesn't pay much attention for these problems, however the patients neither ask for help ("the physician is already too busy", "there is nothing to do").
- Standardized protocols for the management of late effects are rarely used



CLINICAL NEEDS & POSSIBLE SOLUTIONS

- Improved locoregional control
- Higher (disease free) survival
- Less morbidity
- Better quality of life

CLINICAL NEEDS & POSSIBLE SOLUTIONS

- Improved locoregional control
- Higher (disease free) survival
- Less morbidity
- Better quality of life
- Higher conformal radiotherapy
- Faster treatment delivery
- Patient tailored/Risk stratified
- Minimizing adjustable risk factors
- Optimization and standardization of late effect management
- ...

Artificial Intelligence



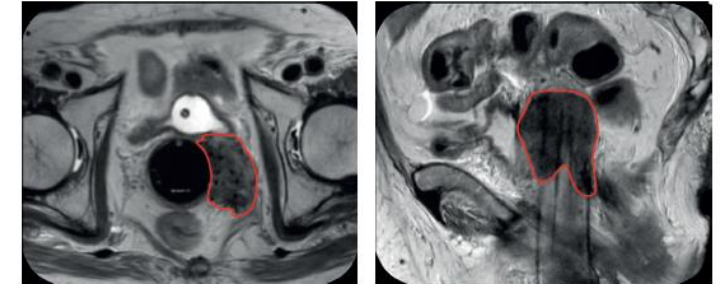
HOW?



Online Adaptive



Advanced Imaging & Planning



Risk factor modification



Late Effect management



Individualized Brachy



Photos of 3D printed applicators, with and without LED backlights.

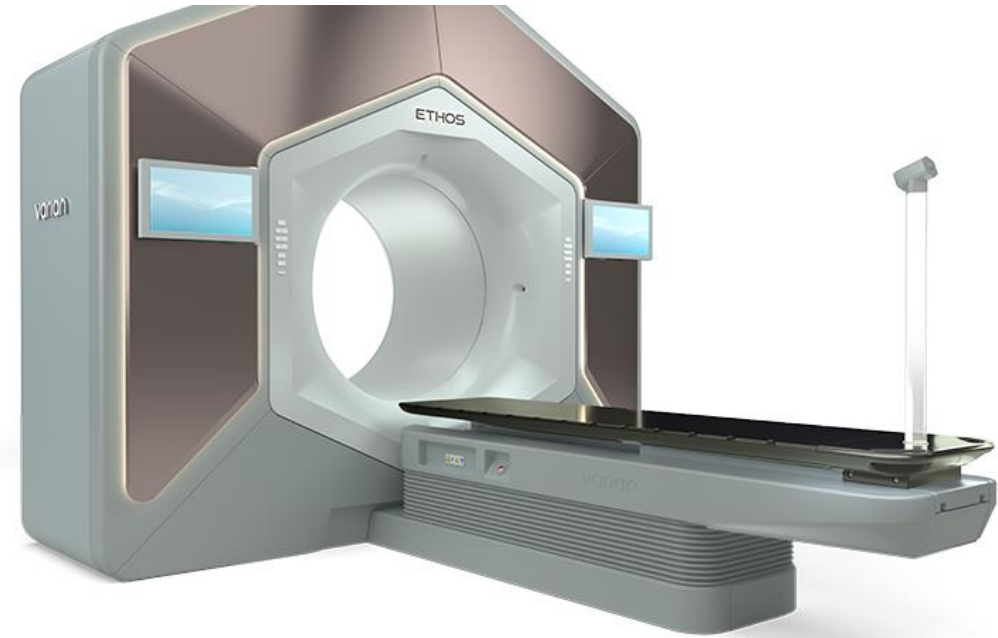
Quality of life



LOCOREGIONAL CONTROL[↑] & MORBIDITY[↓]

Higher conformal: less geographical misses → daily adaptive

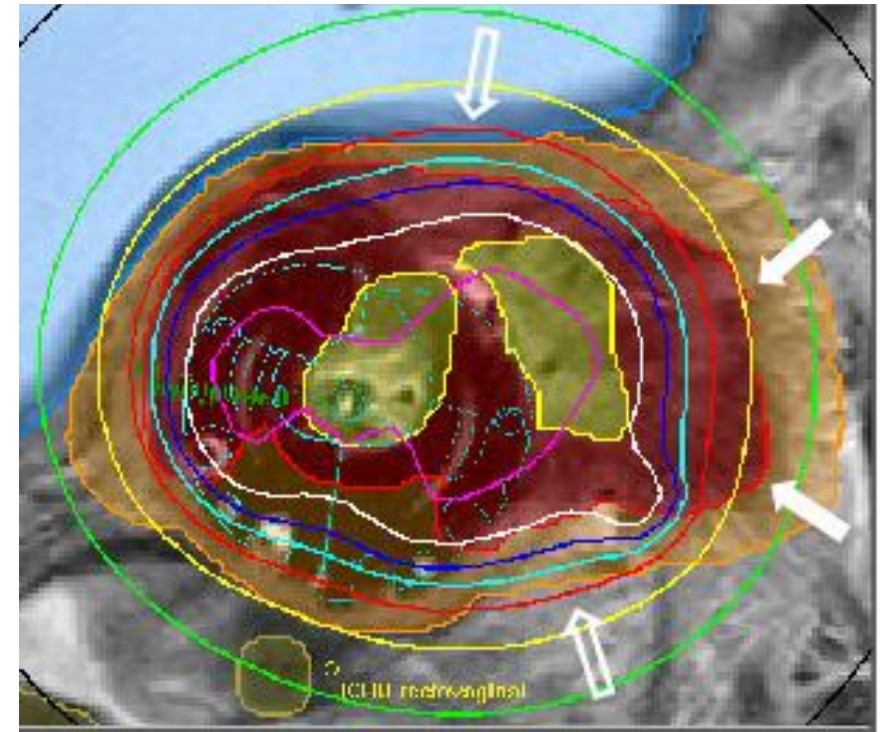
- Every day a new EBRT treatment plan based on the anatomy of the day (“plan of the day”)
- Accounts for target and OAR movements



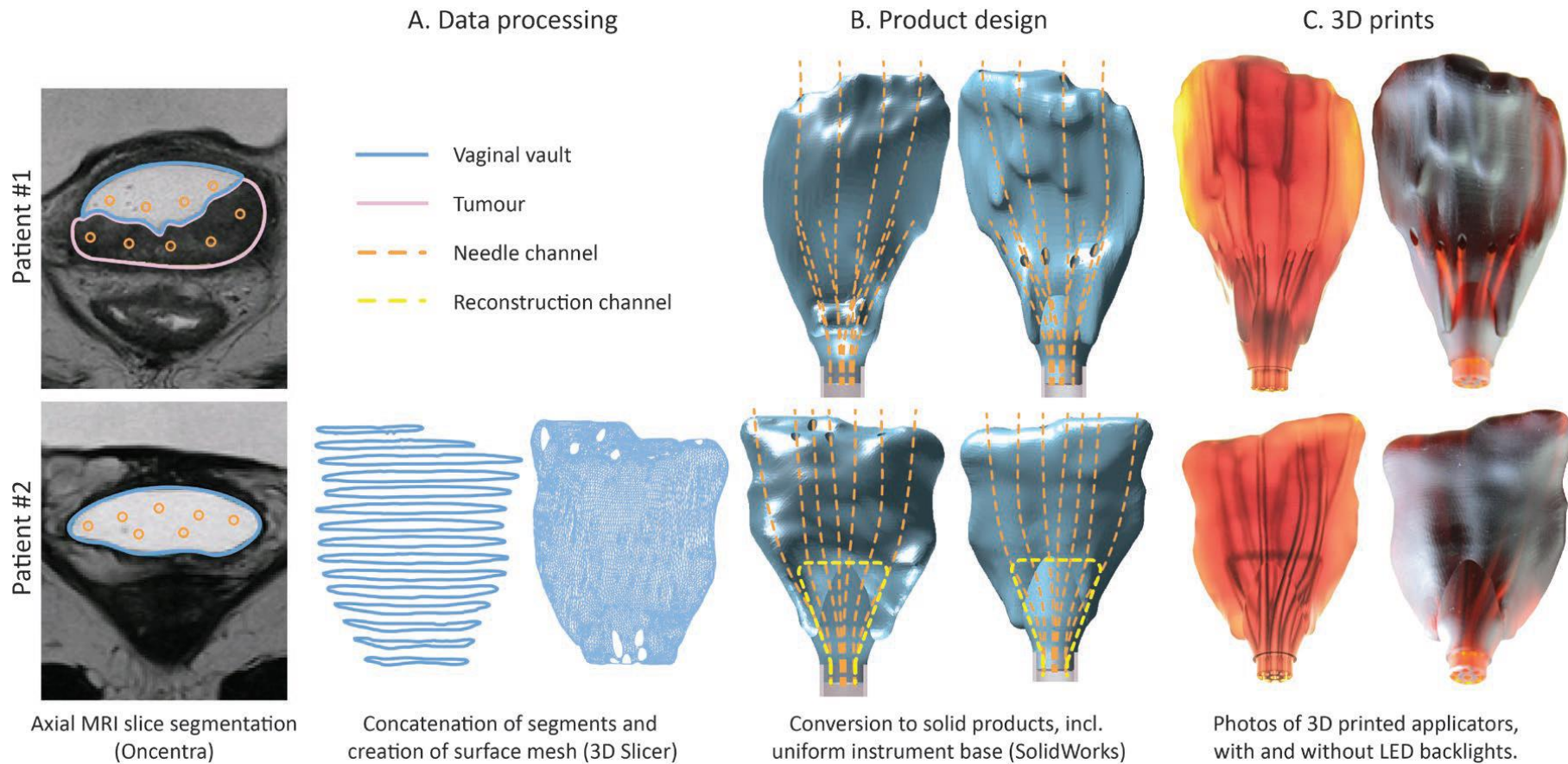
LOCOREGIONAL CONTROL↑ & MORBIDITY↓

Higher conformal – one size ≠ fits all

- ARCHITEC project: Adaptive Brachytherapy using Customised Needle Applicators
- Aims: to optimize treatment conformity in locally advanced tumors with **3D-printed patient-tailored applicators** that include spatially optimized needle source channels

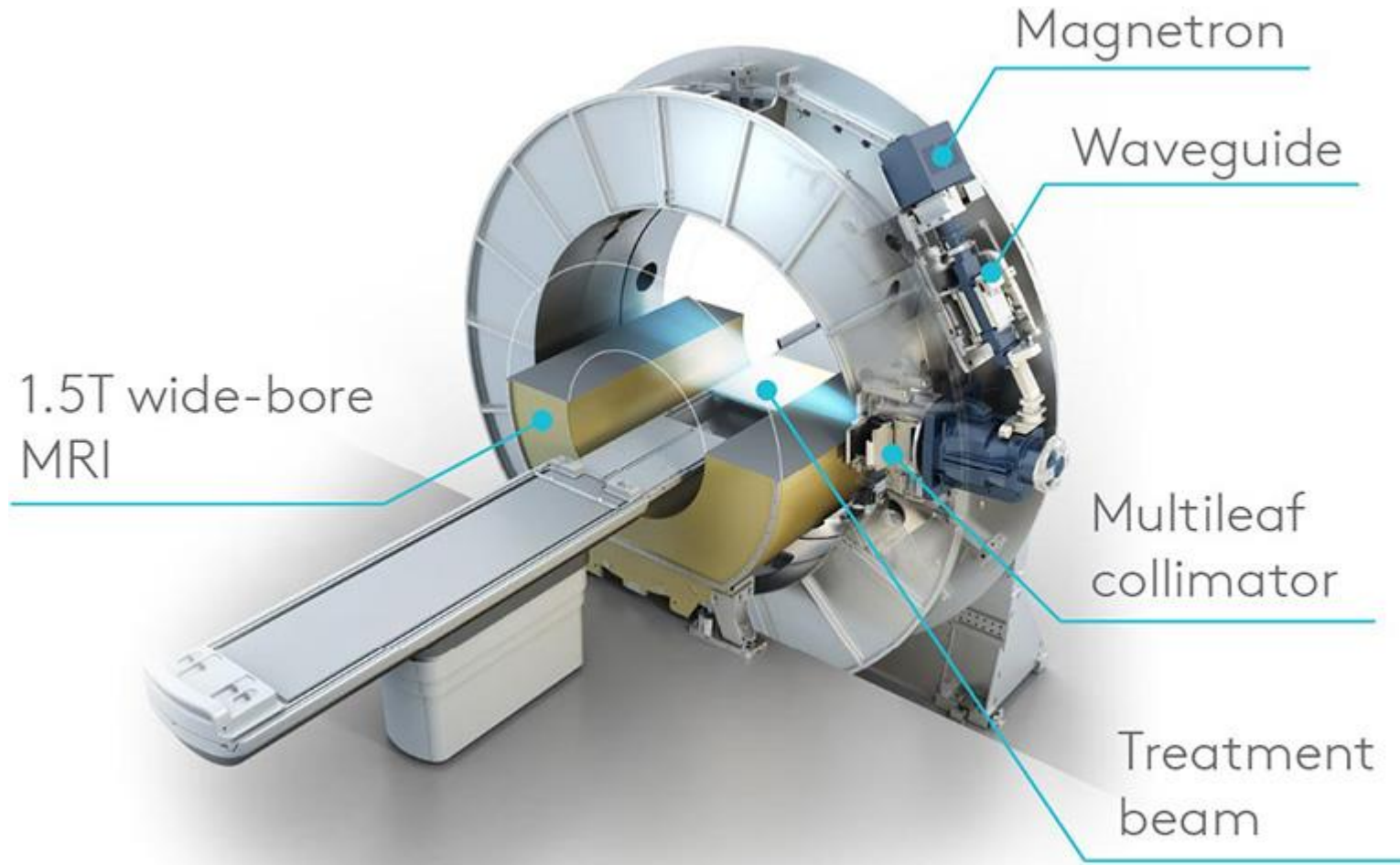


PERSONALIZED BRACHYTHERAPY



MR-LINAC

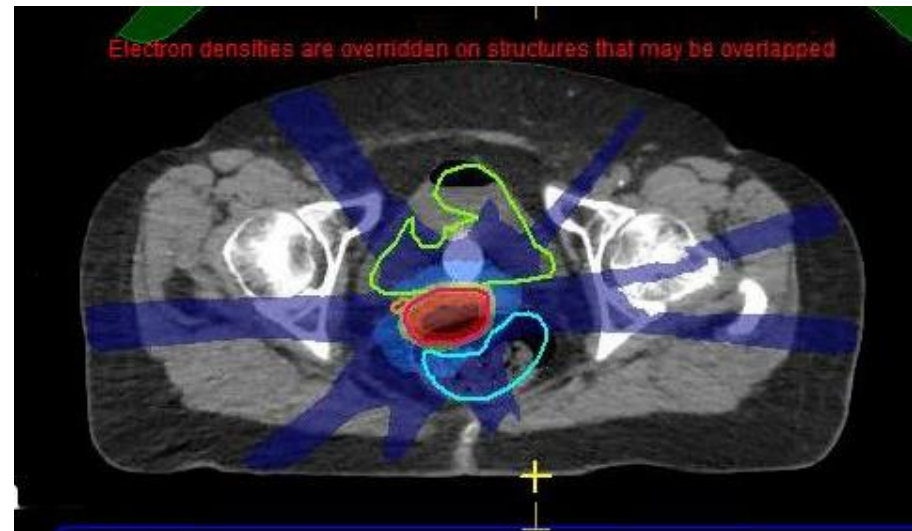
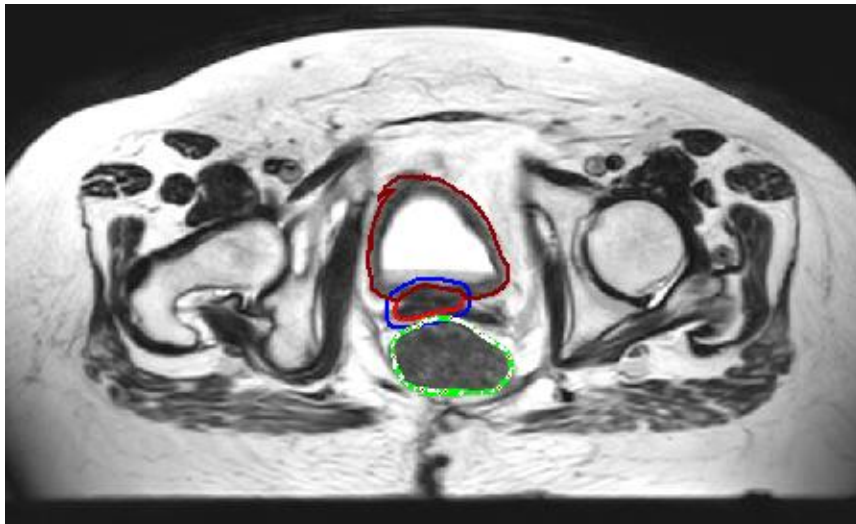
In case Brachytherapy boost is not feasible



MR-LINAC

In case Brachytherapy boost is not feasible

- Good visualization of tumor and surrounding organs
- Dose distribution can be adapted to daily anatomy
- Dose levels close to brachytherapy may be achievable
- However... small field of view, thus large field not suitable



LESS MORBIDITY – PROTON THERAPY

PROTECT: Prospective Phase-II-Trial Evaluating Adaptive Proton Therapy for Cervical Cancer

- **Aim:** evaluate the differences in side effects between photon therapy and proton therapy, both combined with chemotherapy, for locally advanced cervical cancer.
- 30 patients needed: 15 treated with photon therapy, and 15 treated with proton therapy
- Evaluation of dose to OARs, toxicity, impact on immune response

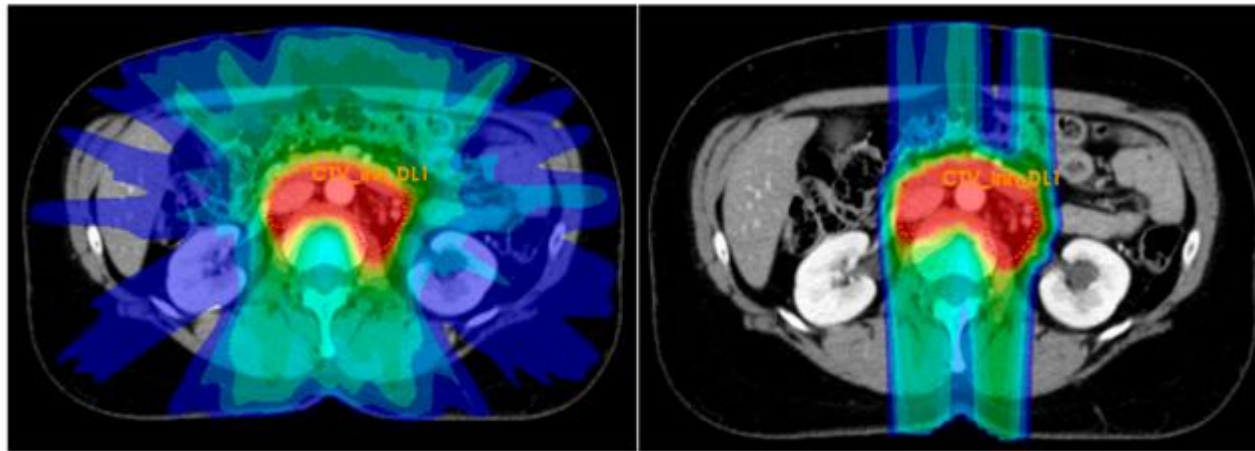
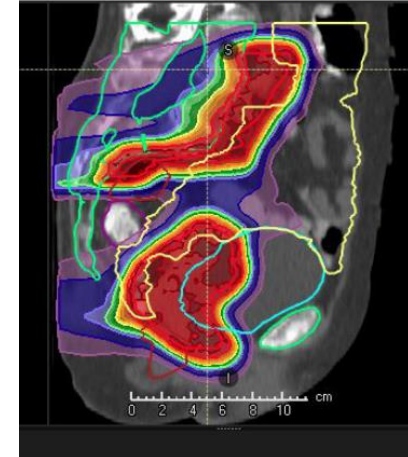
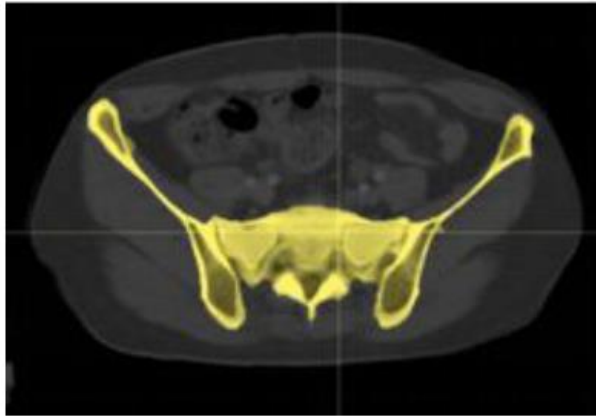


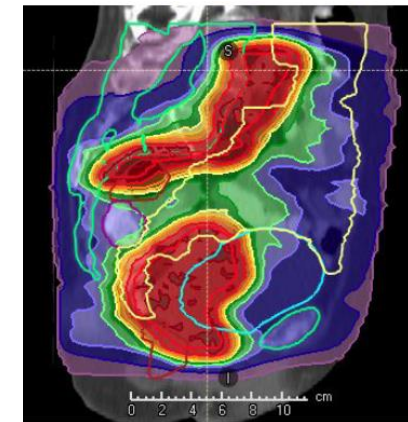
Figure 1. A typical dose distribution for the para-aortic region for IMRT (left) and IMPT (right) [24].

LESS MORBIDITY – BONE MARROW SPARING

PROTECT: BM sparing with VMAT vs. IMPT



IMPT



VMAT

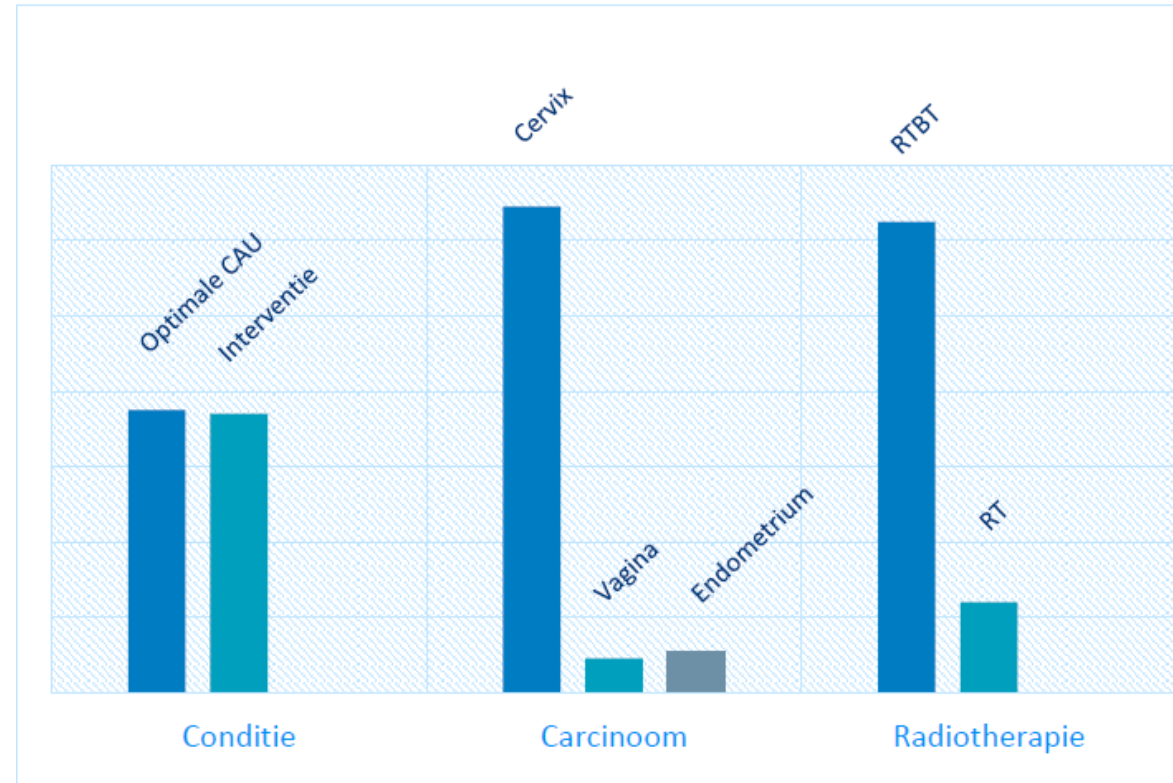
Dosimetric parameter	Number of studies finding significant results number of studies including dosimetric parameter		
	LSS	LOW	Ilium
V5	0/1 (0%)	1/1 (100%)	0/1 (0%)
V10	1/6 (17%)	1/5 (20%)	0/5 (0%)
V15	0/1 (0%)	0/1 (0%)	0/1 (0%)
V20	1/5 (20%)	2/5 (40%)	1/5 (20%)
V30	0/5 (0%)	0/5 (0%)	0/5 (0%)
V40	0/4 (0%)	0/4 (0%)	0/4 (0%)
V45	0/1 (0%)	0/1 (0%)	0/1 (0%)
Dmean	1/2 (50%)	0/1 (0%)	1/1 (100%)

With courtesy of Sander Kuipers

BETTER QOL

SPARC: Seksuele revalidatie na radiotherapie voor gynaecologische kanker

- Randomised study
- Closed dec 2022
- > 220 patients included
- First results expected end 2023



BETTER QOL – LATE EFFECT MANAGEMENT ELEGANT

- Started in 2017
- Structured assesment and management of (severe) late effects
- Monthly multidisciplinary board



The screenshot shows the website for the Expertisecentrum Late Effecten Gynaecologische kanker Amsterdam (ELEGANT). The header includes navigation links for 'Zorg', 'Educatie', and 'Research', along with the 'Amsterdam UMC' logo and location information: 'Locatie AMC | Meibergdreef' and 'Locatie VUmc | De Boelelaan'. The main title is 'Expertisecentrum Late Effecten Gynaecologische kanker Amsterdam (ELEGANT)'. Below this, a paragraph describes the center's mission: 'De behandeling van gynaecologische kanker kan op lange termijn nare bijwerkingen hebben. Veel vrouwen hebben last van hun darmen of hun blaas, of ze kampen met seksuele problemen. Het expertisecentrum ELEGANT (Expertisecentrum Late Effecten Gynaecologische kAnker AmSTerdam) biedt zorg aan vrouwen die last hebben van bijwerkingen van hun behandeling voor gynaecologische kanker.' To the right of the text is a photo of two people in a consultation. Below the text, contact information is provided: '020 566 4344', 'E-mail: elegant@amc.nl', and a link '<< Zorg bij kanker'. At the bottom, there are three columns of links. The first column, 'Klachten', lists 'Darmklachten', 'Psychische klachten', 'Plasklachten', and 'Seksuele klachten' with corresponding icons. The second column, 'Wat doen wij', has a link to 'Specialistenteam' with a photo of the team. The third column, 'Meer informatie', has a link to 'Websites' with a globe icon.

Locatie AMC | Meibergdreef Locatie VUmc | De Boelelaan

Zorg Educatie Research

Amsterdam UMC
Universitair Medische Centra

Expertisecentrum Late Effecten Gynaecologische kanker Amsterdam (ELEGANT)

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<< Zorg bij kanker

Klachten

- Darmklachten
- Psychische klachten
- Plasklachten
- Seksuele klachten

Wat doen wij

- Specialistenteam

Meer informatie

- Websites

BETTER QOL – LATE EFFECT MANAGEMENT

ELEGANT

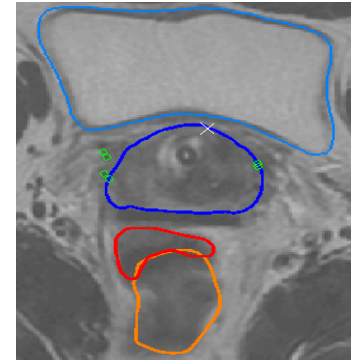
- Started in 2017
- Structured assesment and management of (severe) late effects
- Monthly multidisciplinary board
- > 100 patients
- 65% of the patients have substantially less complaints



AI IN RTH – FAST AUTOMATED PLANNING

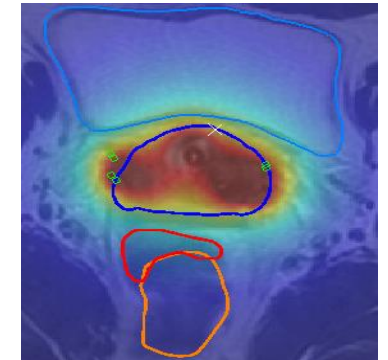
BiCycle

- Wishlist based on protocol and treating physician preference
- Fully automated generation of one treatment plan
- Plan generation takes 20 seconds on average
- Prospective trial nearly finalized
- Planning to implement in daily clinic spring 2023



BiCycle

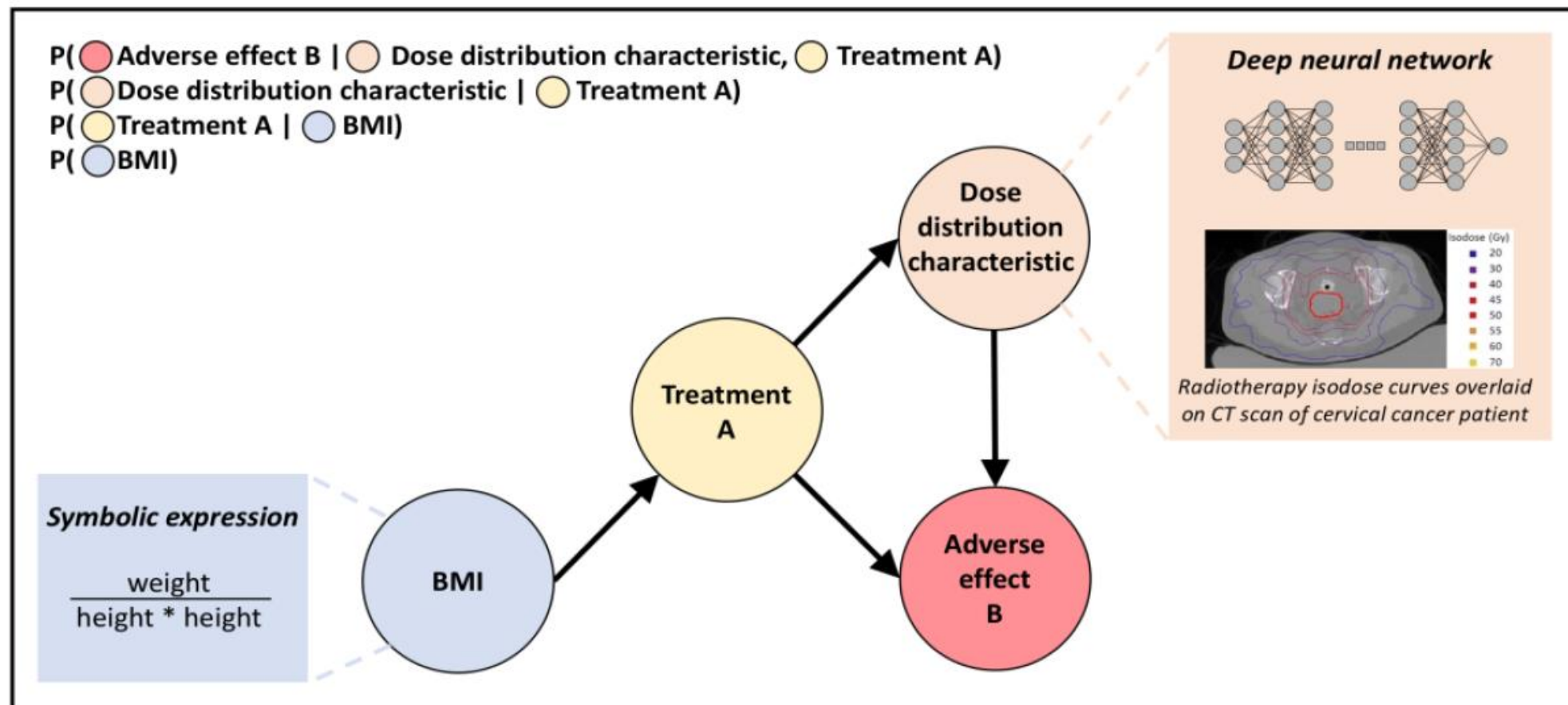
Wishlist



Hard constraints
Prioritized objectives
Dosimetry
Geometry (Dwell time distribution)

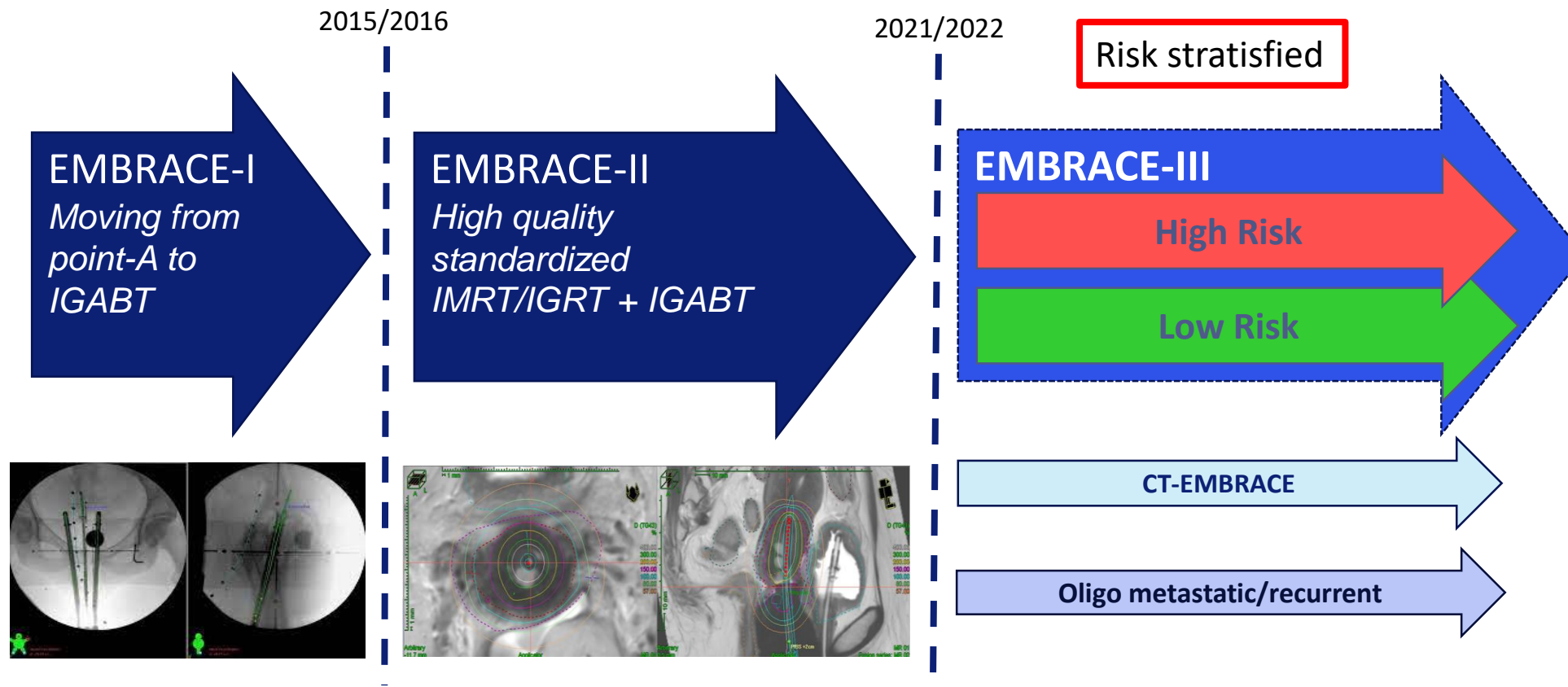
AI IN RTH – PROGNOSTIC MODELS

Examine: Evolutionary eXplainable Artificial Medical INtelligence Engine



EMBRACE STUDIES

From x-ray standard planning → high end image guided radiotherapy
→ risk stratified



Artificial Intelligence



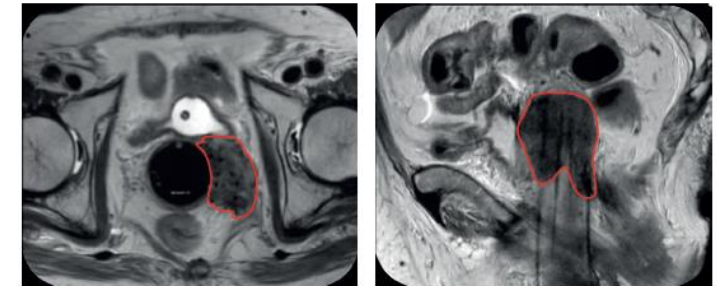
Online Adaptive



Late Effect management



Advanced Imaging & Planning

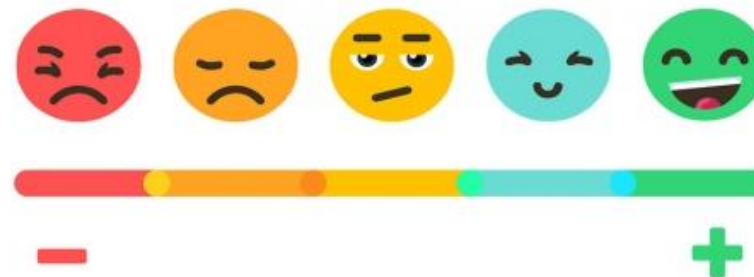


Individualized Brachy



Photos of 3D printed applicators, with and without LED backlights.

Quality of life



Risk factor modification



