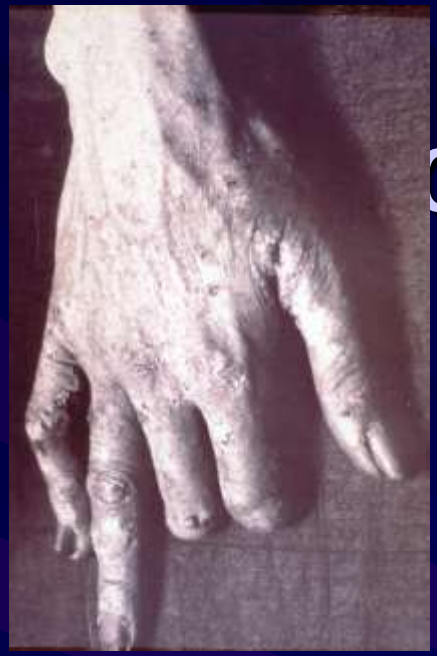
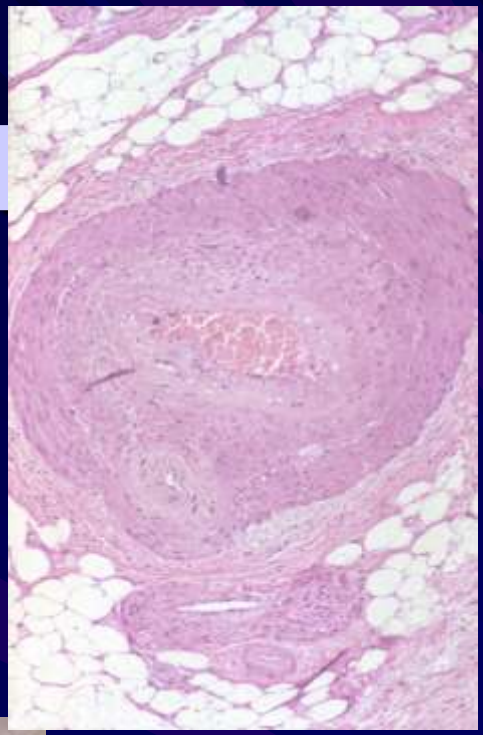
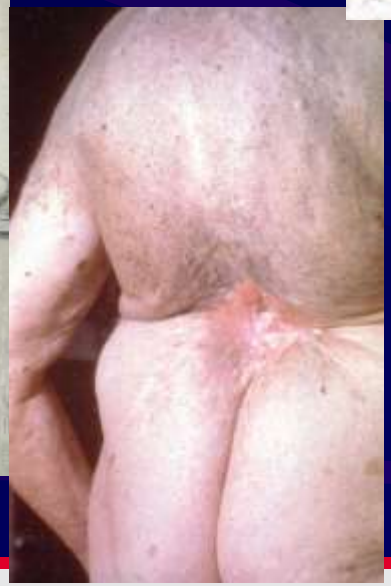
DER BESTRAHLTE DARM- PRÄVENTION UND THERAPIE

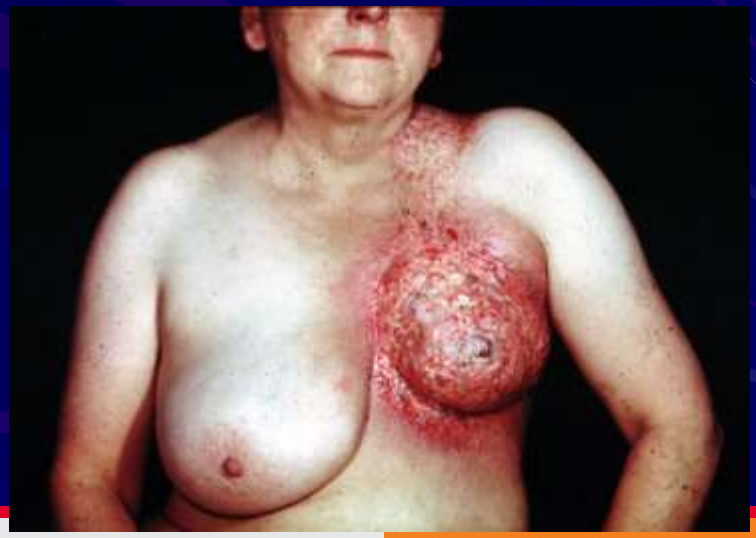
Annemarie Schratter-Sehn

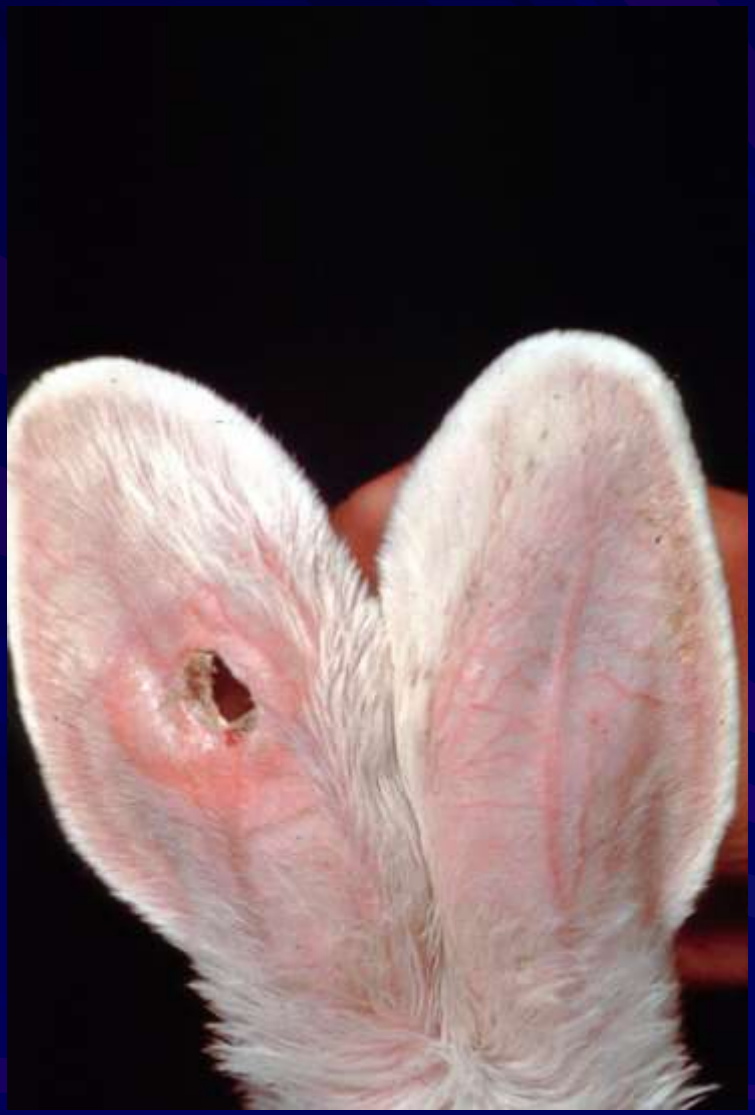
ISDS Malta 2018











RT-NW

Diarrhea

Blutung

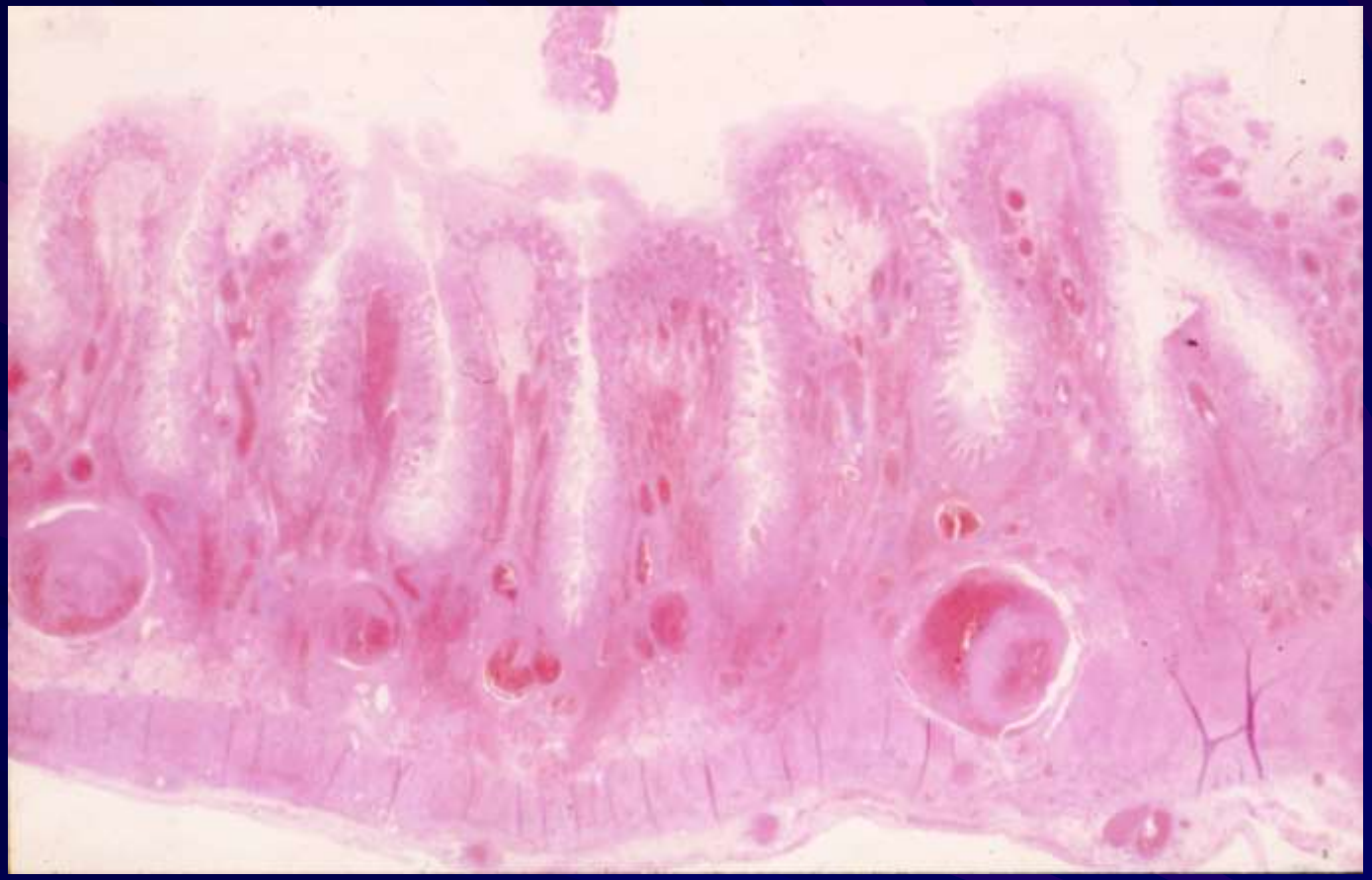
Ulcerationen

Gewichts-Albuminverlust

Fisteln

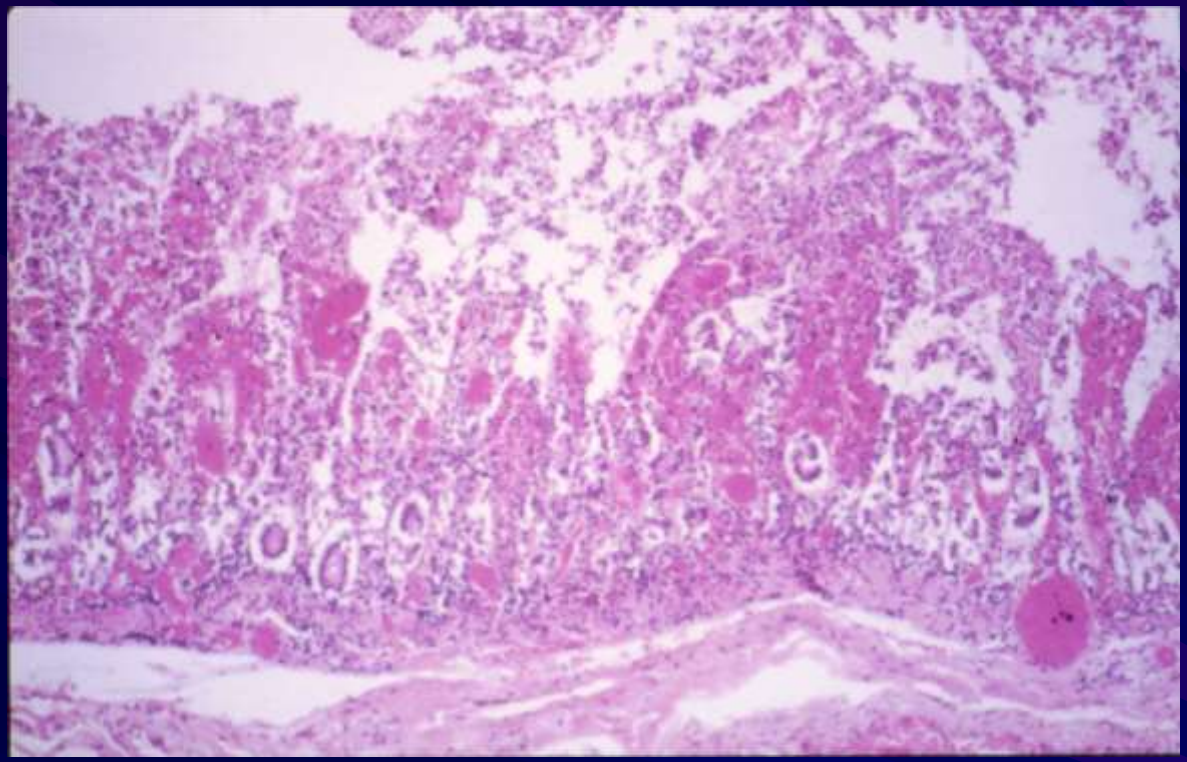
Obstruktionen

Fibrosen



Fenoglio-Preiser / FP94/ acute ischemic damage / small bowel

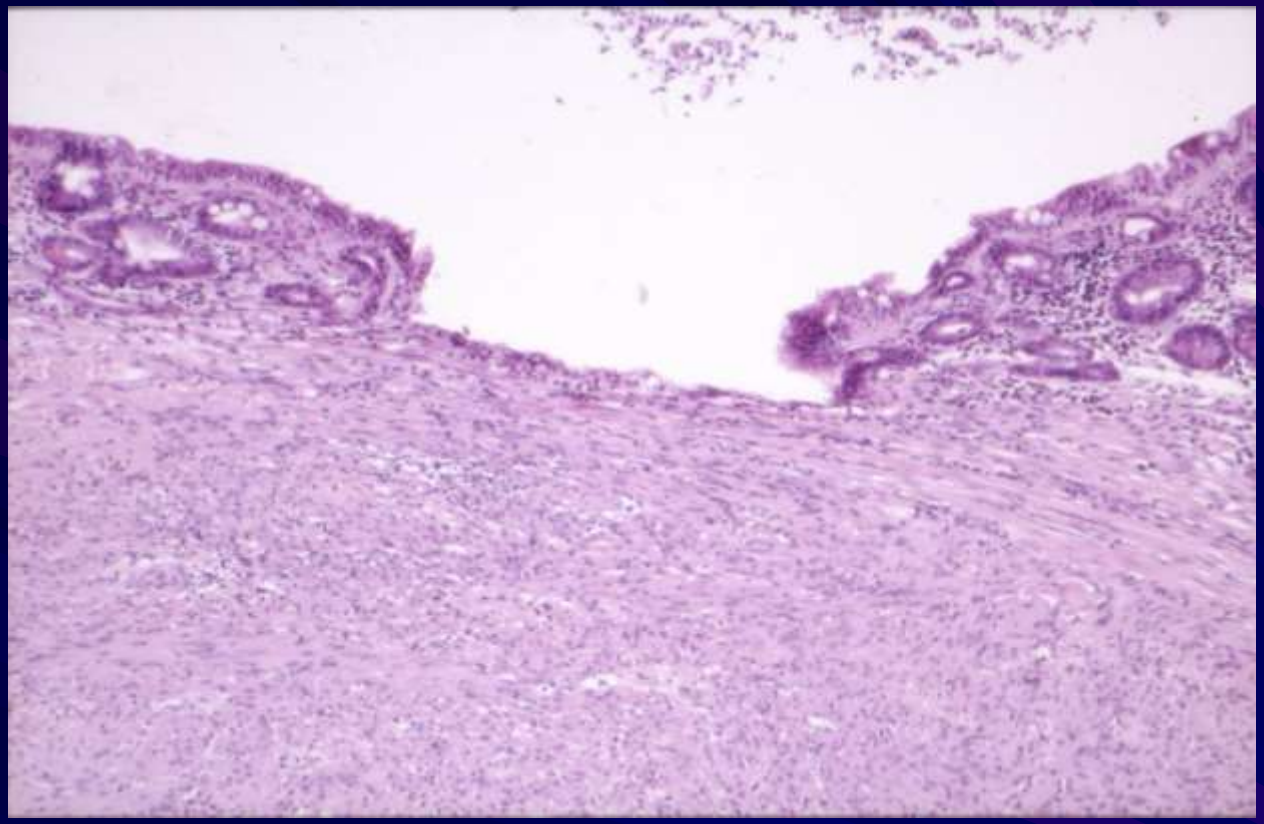
Martin Klimpfinger



Fenoglio-Preiser / FP99/ acute radiation damage / small bowel

M.K

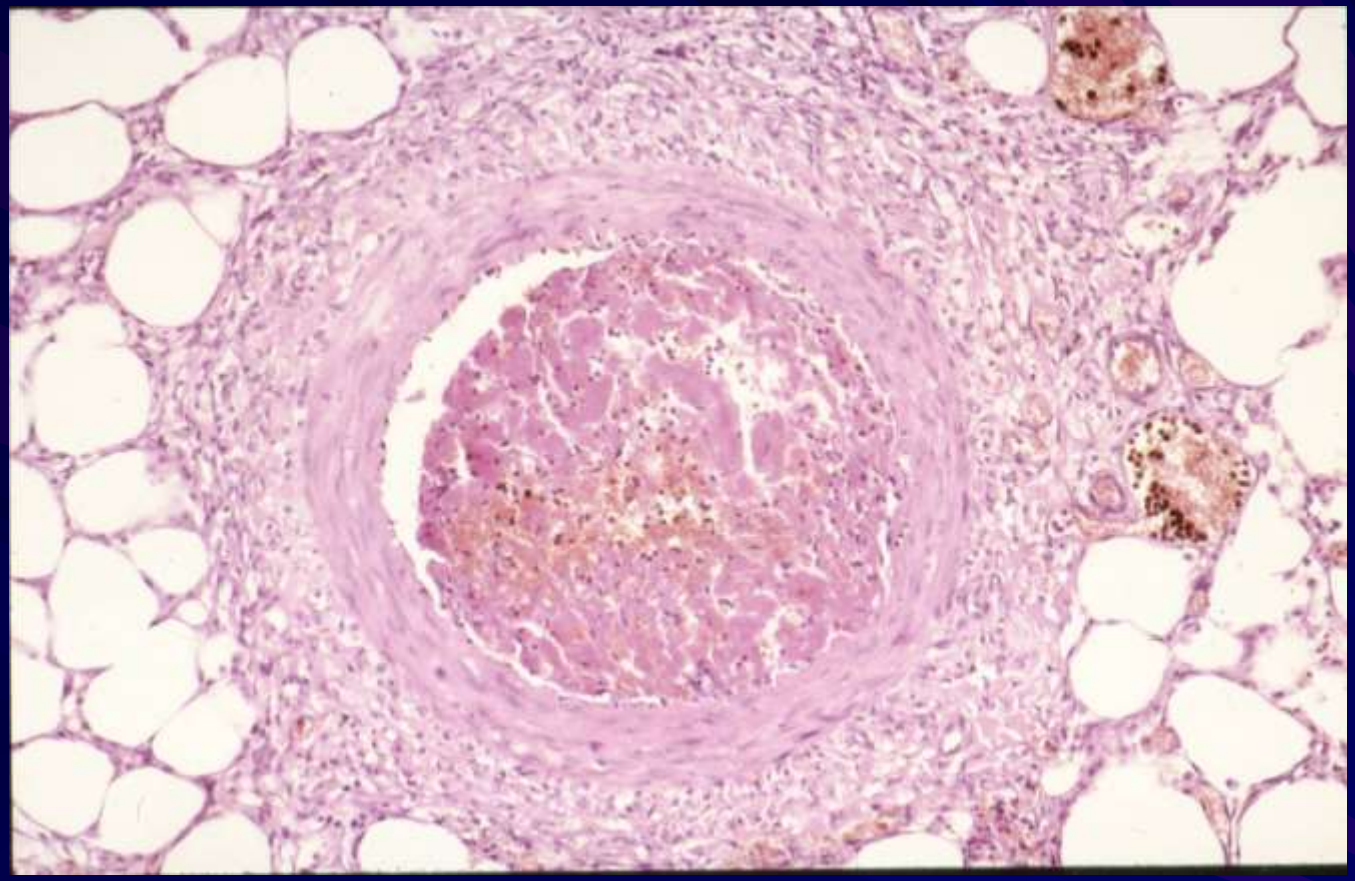
.



Chronisches Ulkus in Abheilung nach Strahlentherapie / Dünndarm

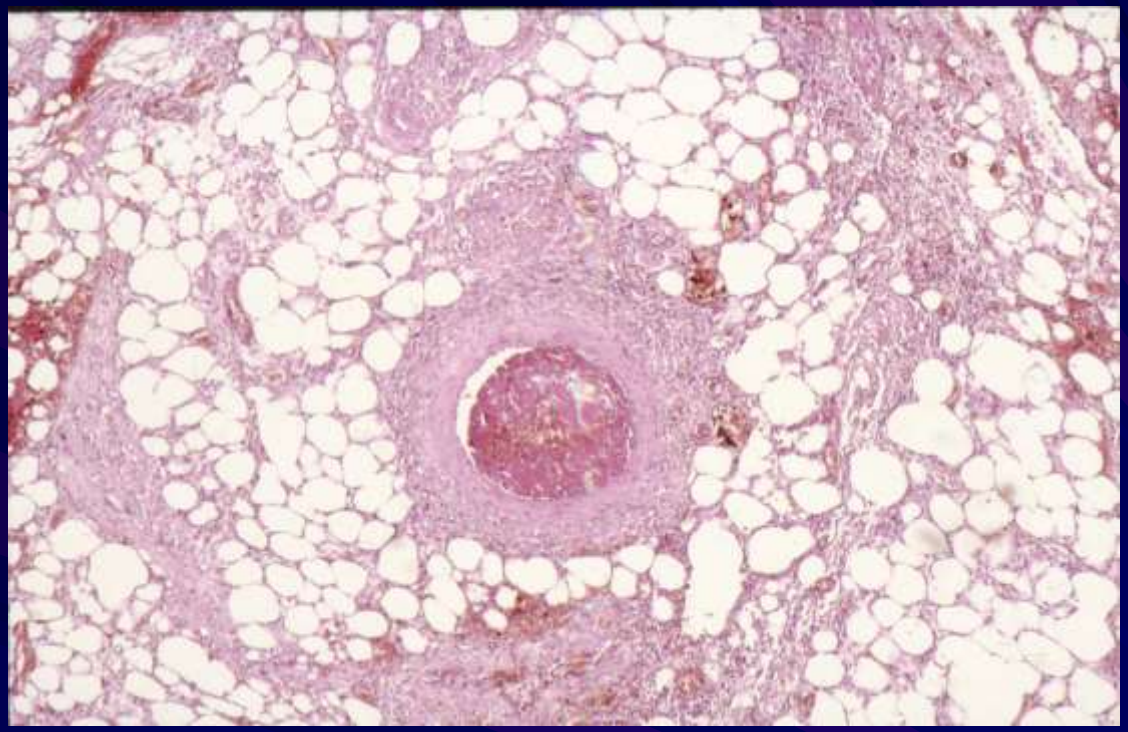
M.K

.



Akute arterielle Gefäßwandveränderungen nach Strahlentherapie

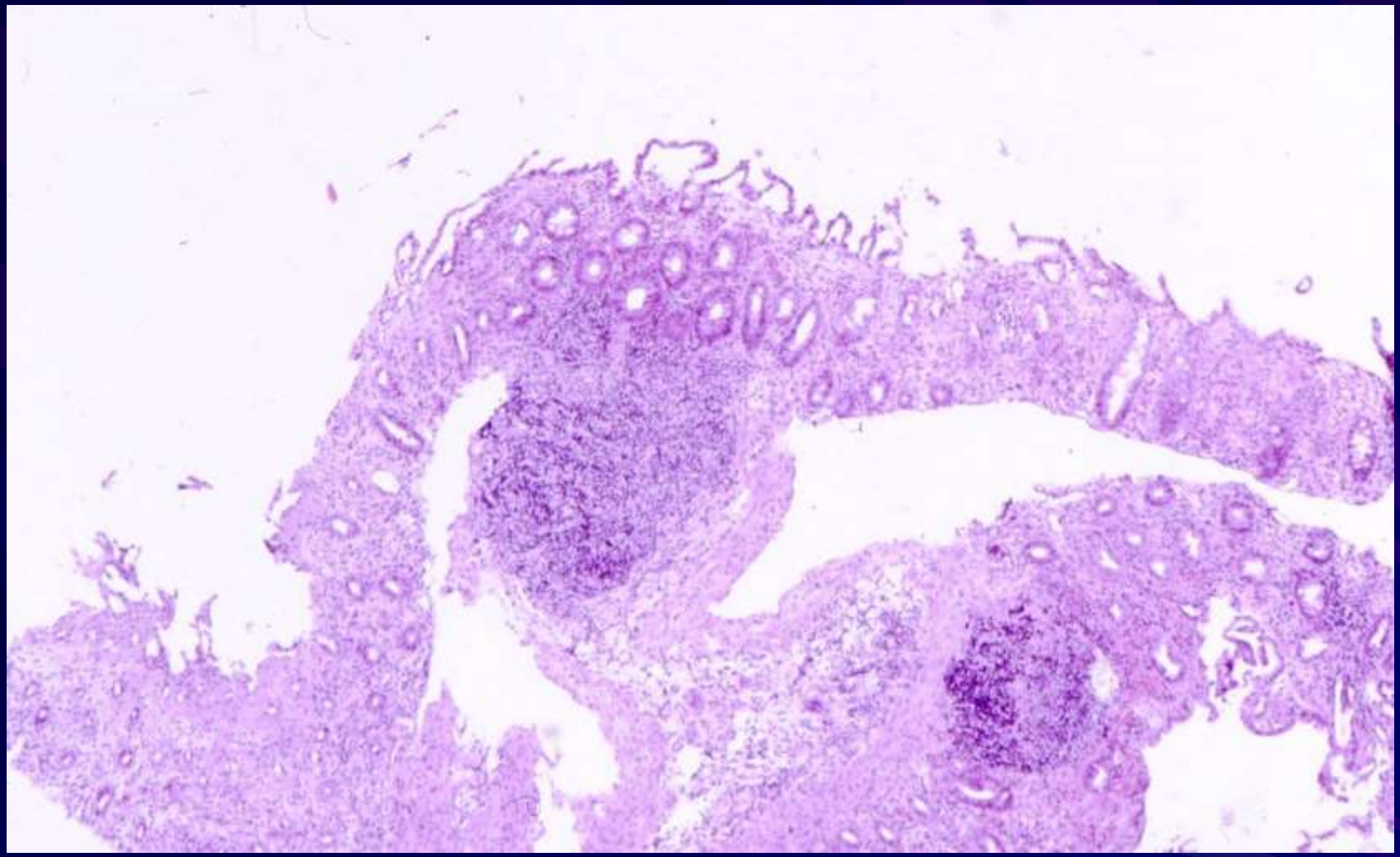
M.K



Akute arterielle Gefäßwandveränderungen nach Strahlentherapie

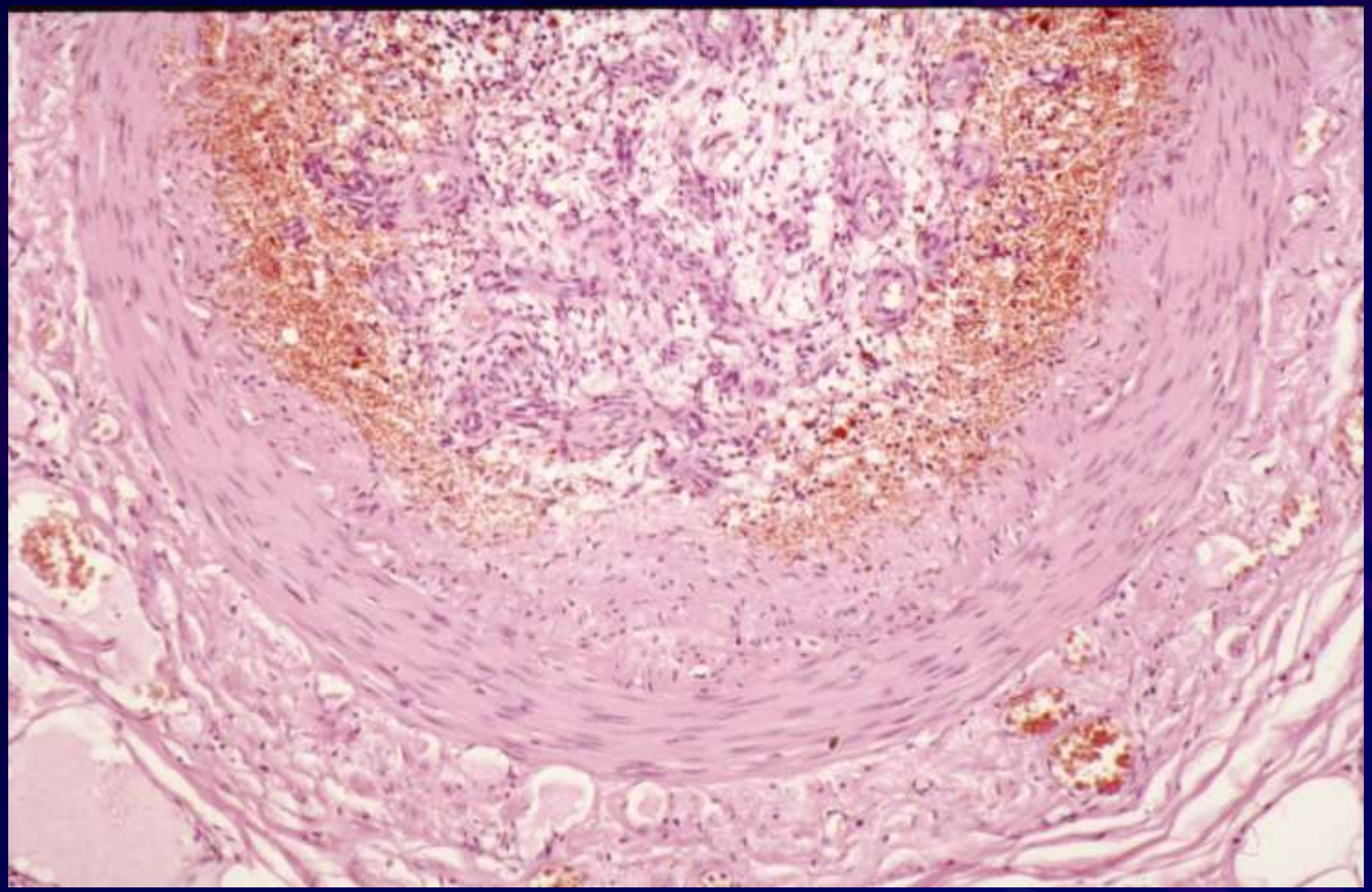
M.K

.

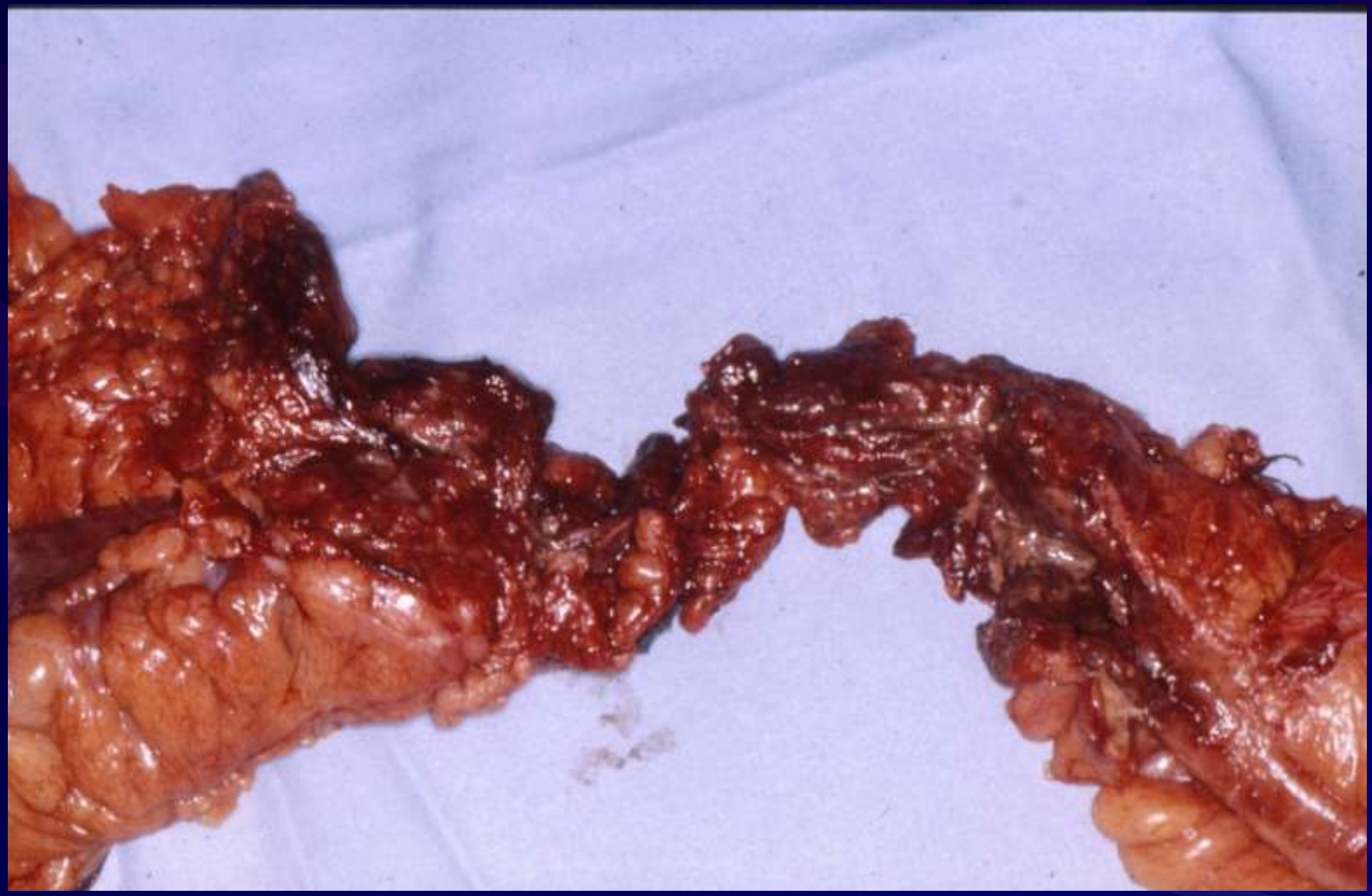


Ischämische Kolitis bei arteriellen Gefäßveränderungen nach Strahlentherapie

M.K



Chronische arterielle Gefäßwandveränderungen nach Strahlentherapie



Perforierte ischämische Kolitis (Op. Prof. Berger / BHB Graz)

M.K

Biologische Grundlagen der Spätfolgen in der Strahlentherapie:

Organtoleranz
Bestrahlungsdosis
Bestrahlungsvolumen
Bestrahlungsfraktionierung
Verstärkungsfaktoren

Bestrahlungsdosen Organtoleranz

SOLIDER TUMOR: 50-80 Gy, 2 Gy/F

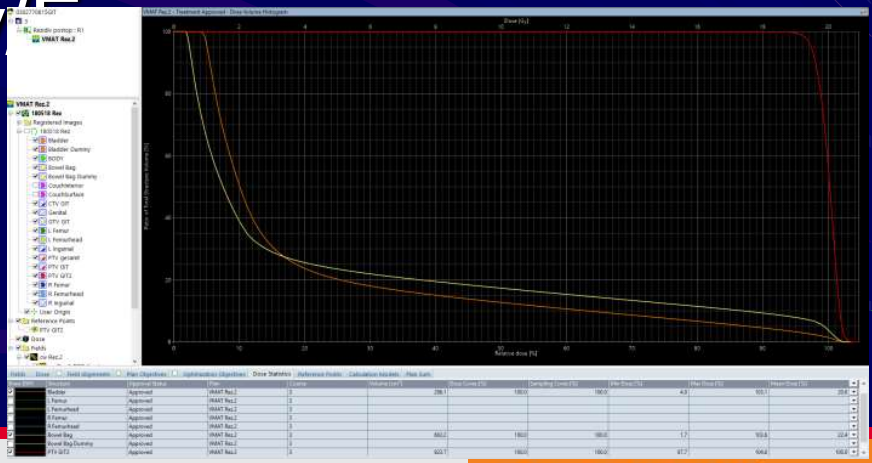
Dünndarm: 20-40 Gy, 2 Gy/F

Dickdarm: 30-50 Gy, 2 Gy/F

Leber: max. 30 Gy, 2 Gy/F

Nieren: max.18 Gy, 2 Gy/F

Dosis-Volumen-Histogramm



QUNTEC DOSE CONSTRAINS

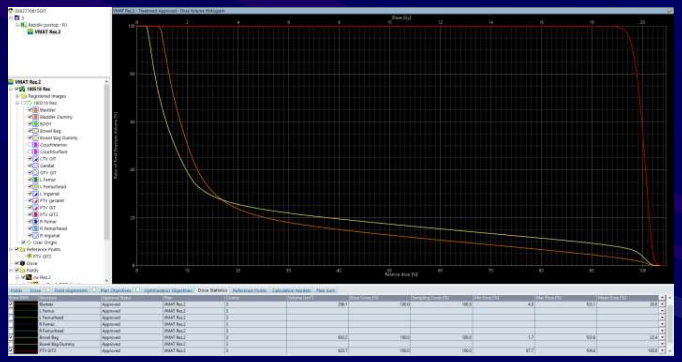
Dosis-Volumen und Fraktionen

Dünndarm

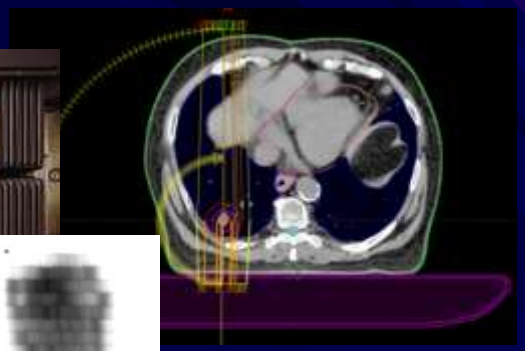
Keine NW: 15 GY Dosis- <120cc Volumen

Keine schweren NW: 45 GY Dosis- <195cc Volumen

SBRT 1F: 12,5 GY Dosis- < 30cc Volumen



Int.J.ROBP Vol.76, No.3pp.S 101-S 107, 2010 BD Kavanagh et al



Teletherapie

Konformale RT

IMRT (IntensitätsModulierte RT)

V-MAT (Volumetric Modulated Arc Therapie)

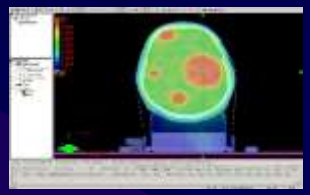
Stereotaxie

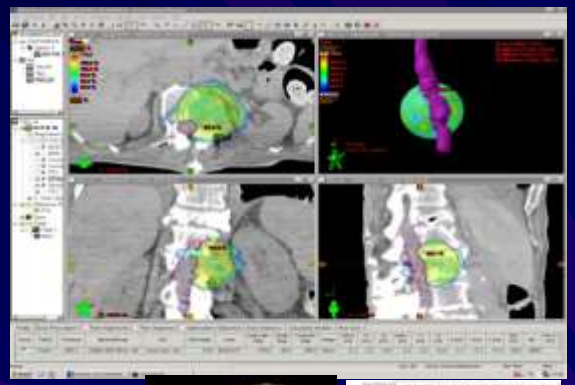
SIB-IMRT-VMAT (Simultan Integrierter Boost)

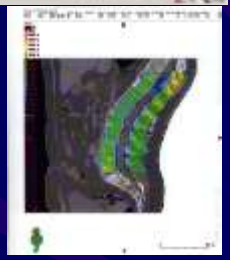
SIS-IMRT-VMAT (Simultan Integriertes Sparing)

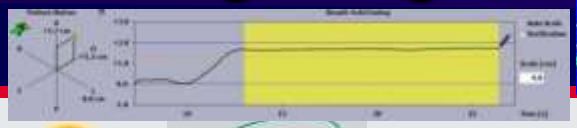
IGRT (Image-guided radiation therapy)

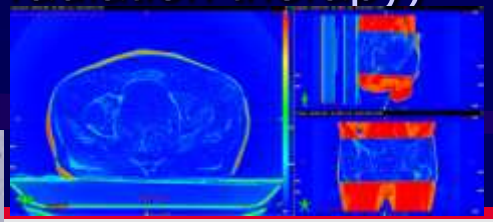
Atemgating

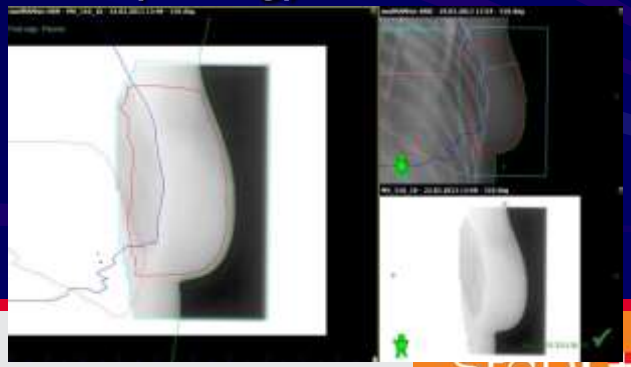


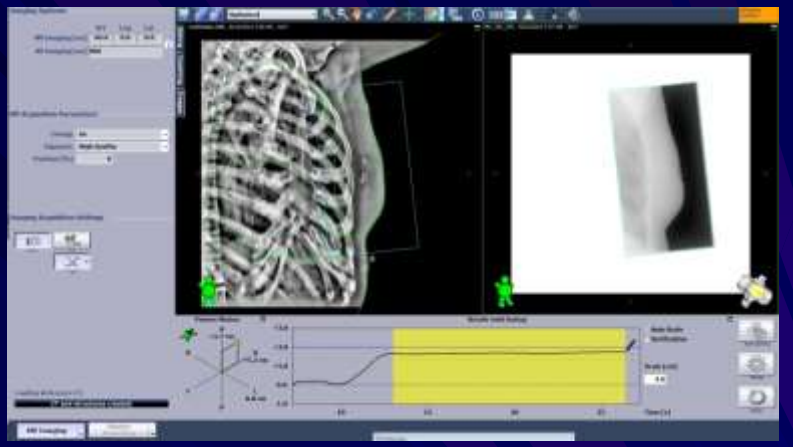


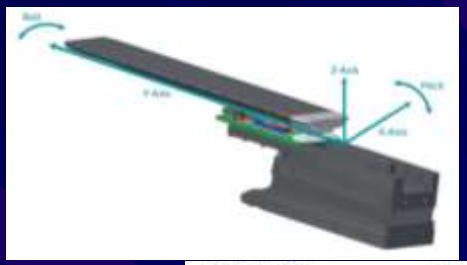


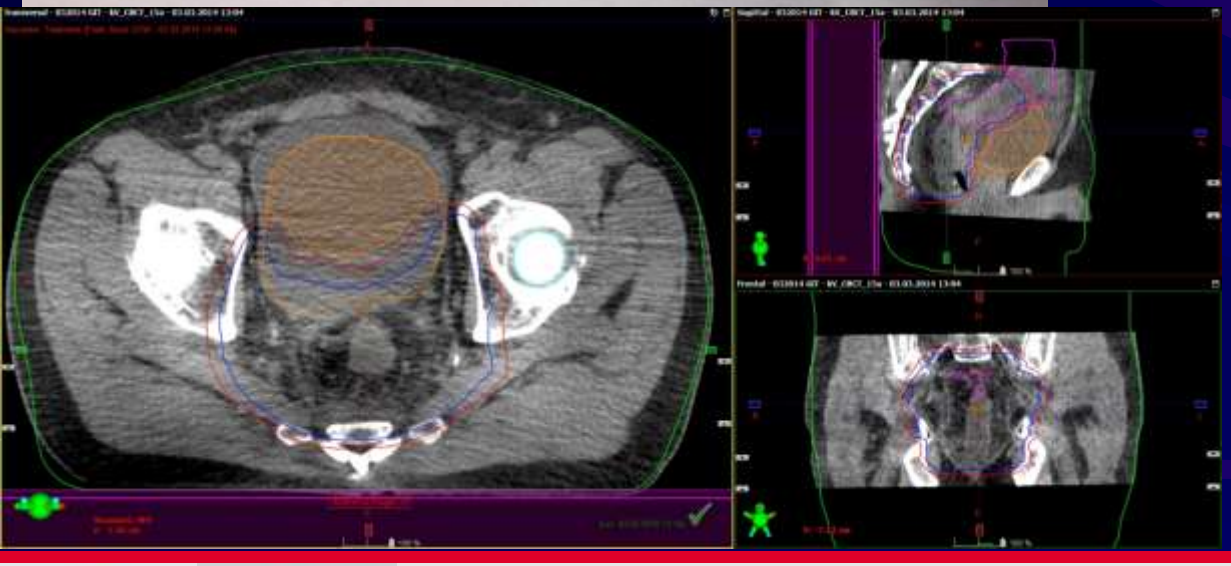












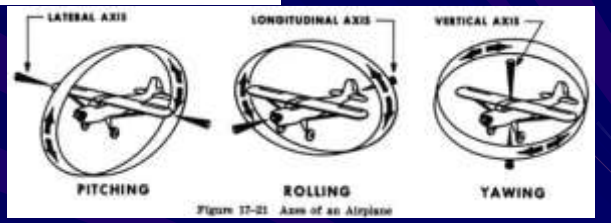
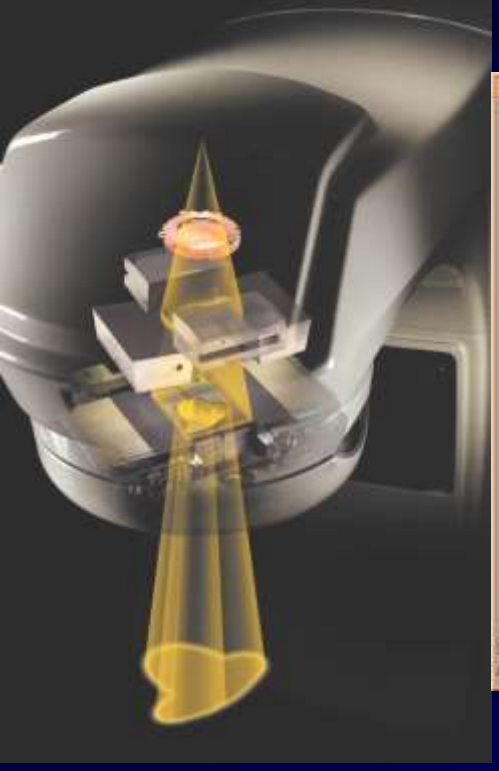
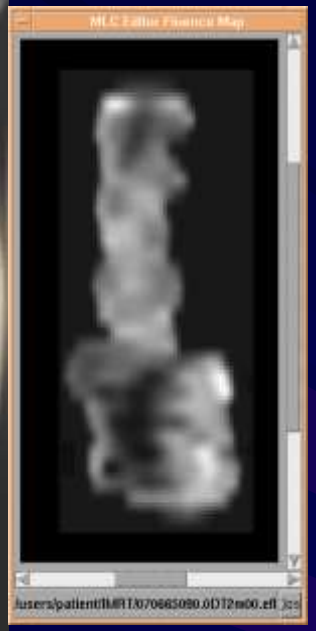
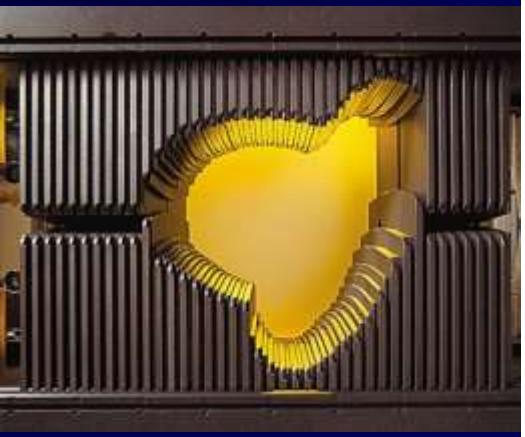
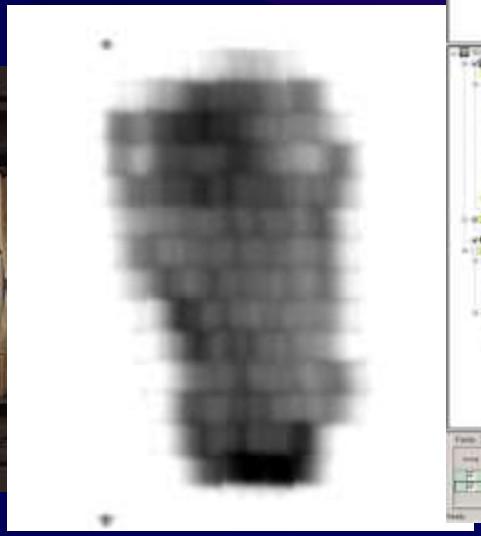


Figure 17-21 Axes of an Airplane



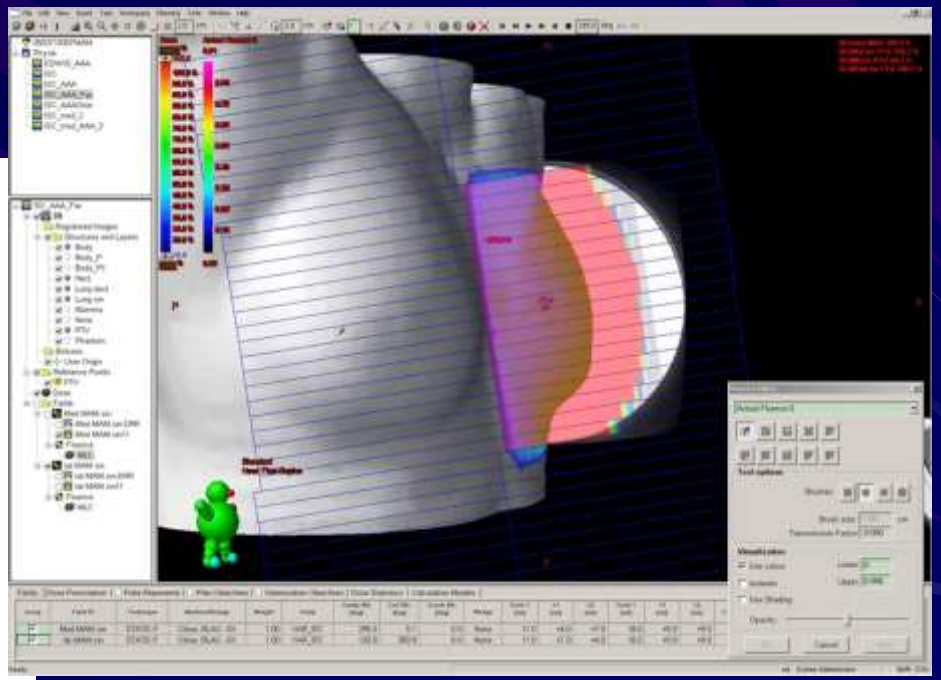


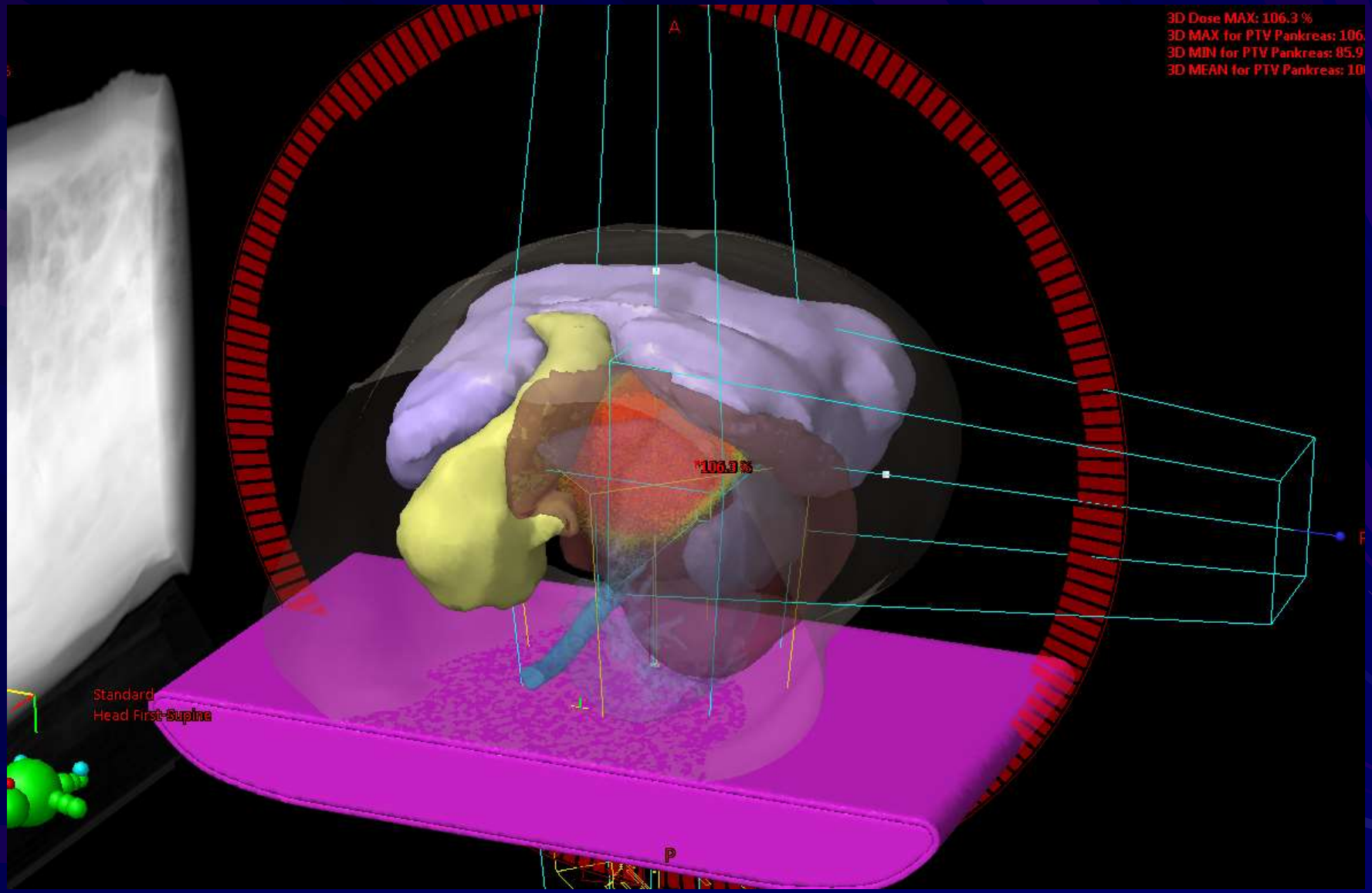


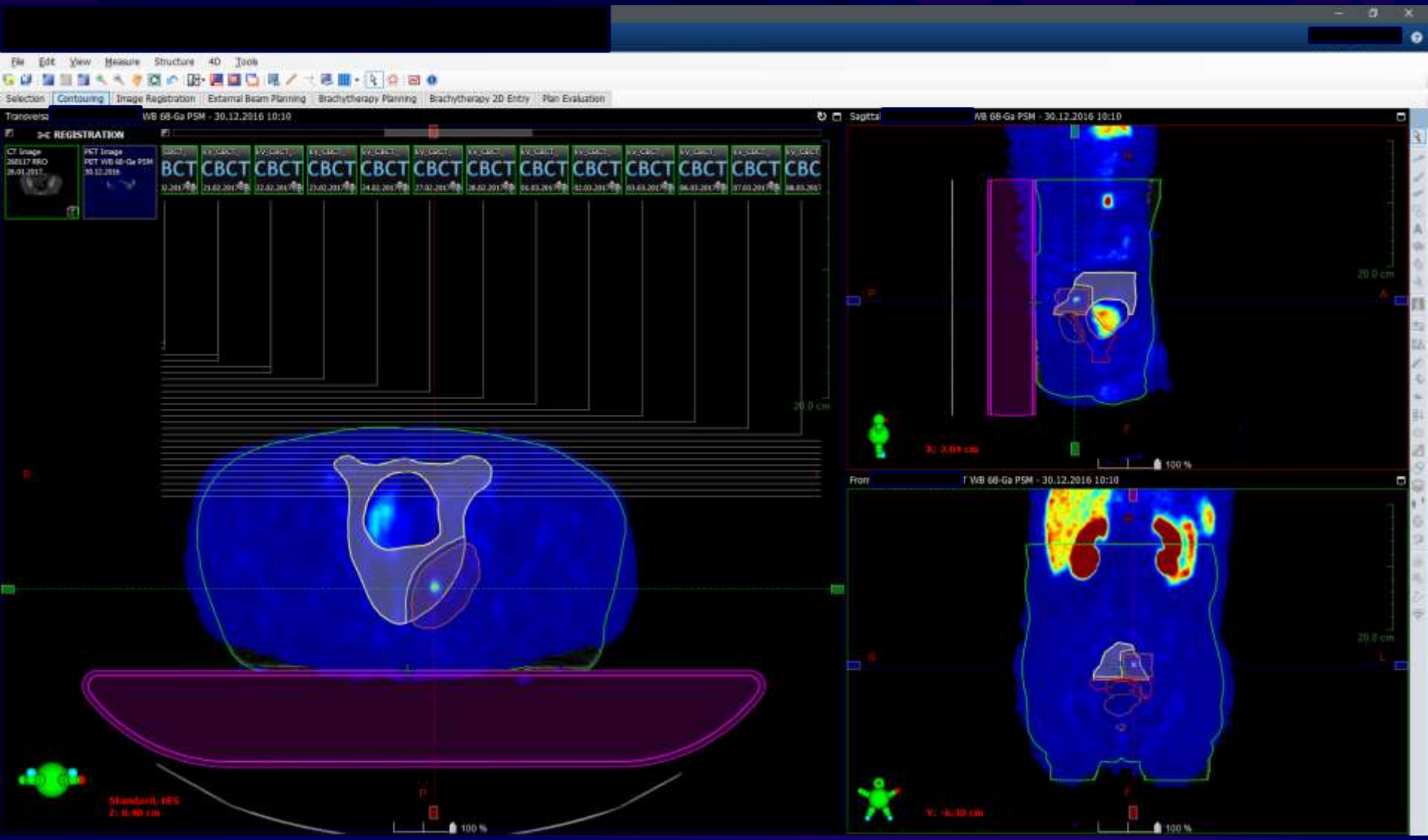


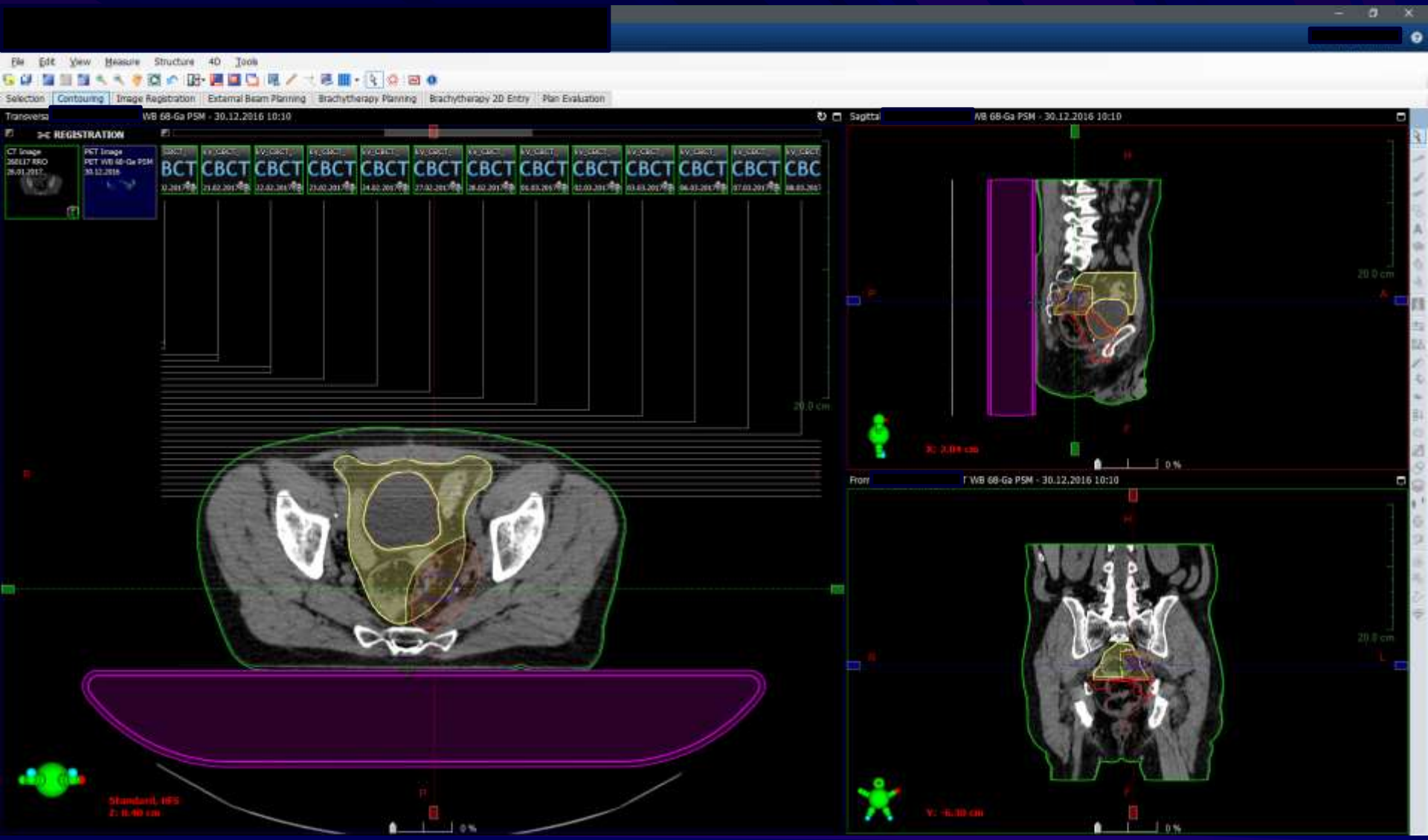
ISC/IMRT/VMAT

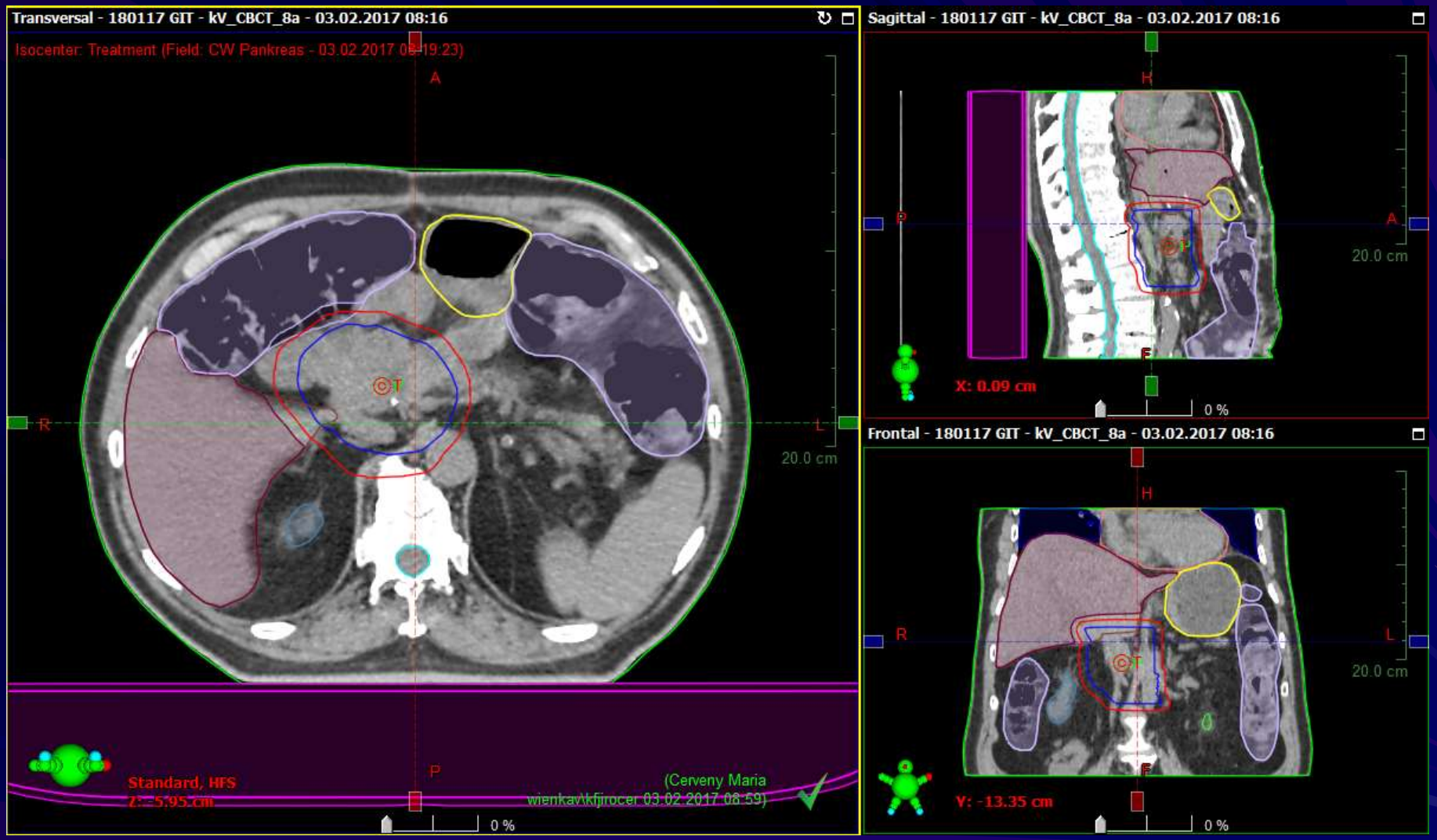
DOSISOPTIMIERUNG im Zielgebiet
DOSISHOMOGENISIERUNG
RISIKOORGANDOSISREDUZIERUNG
KOMPLEXE PLANUNG
KOMPLEXE BESTRAHLUNGSTECHN

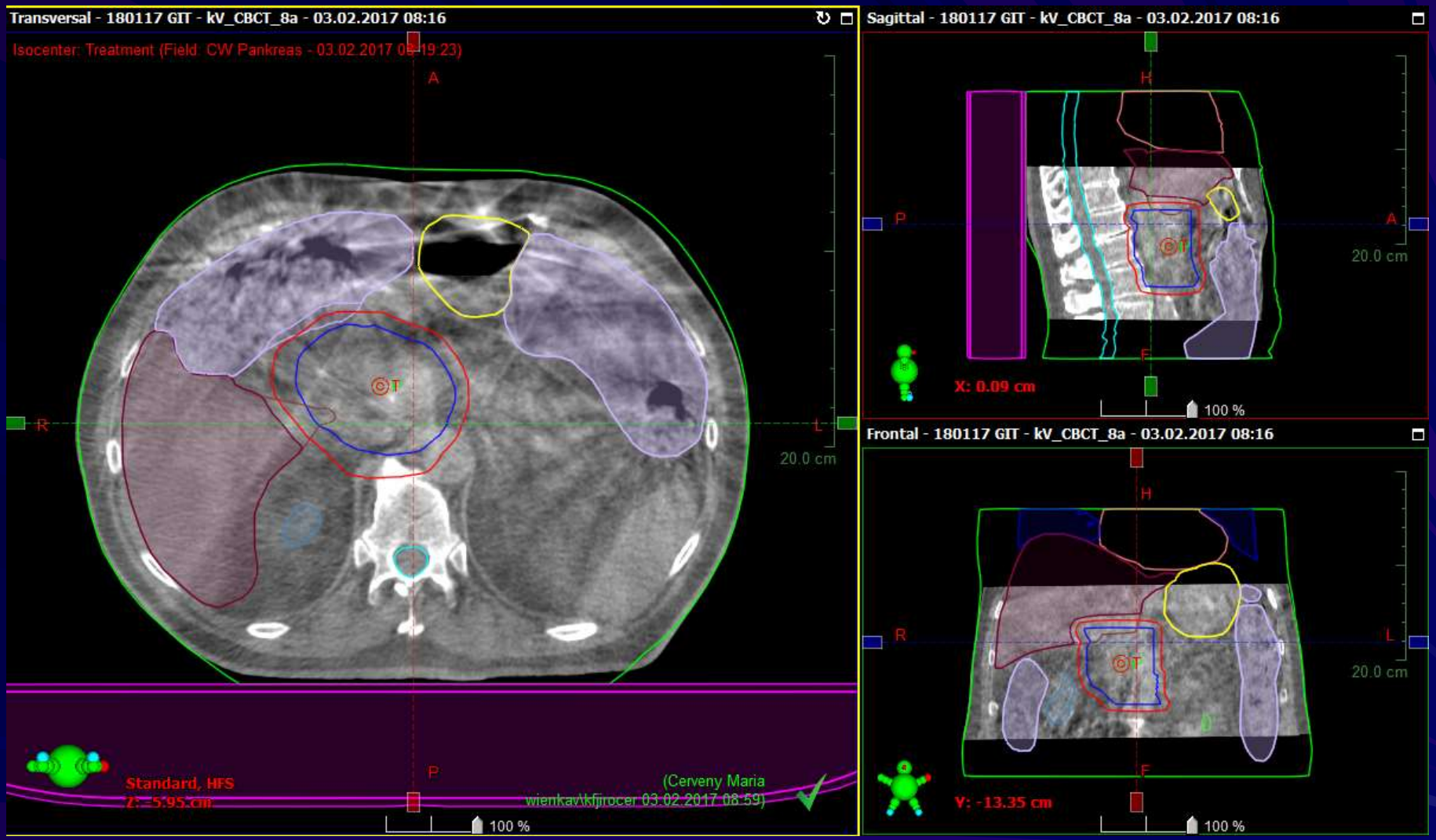


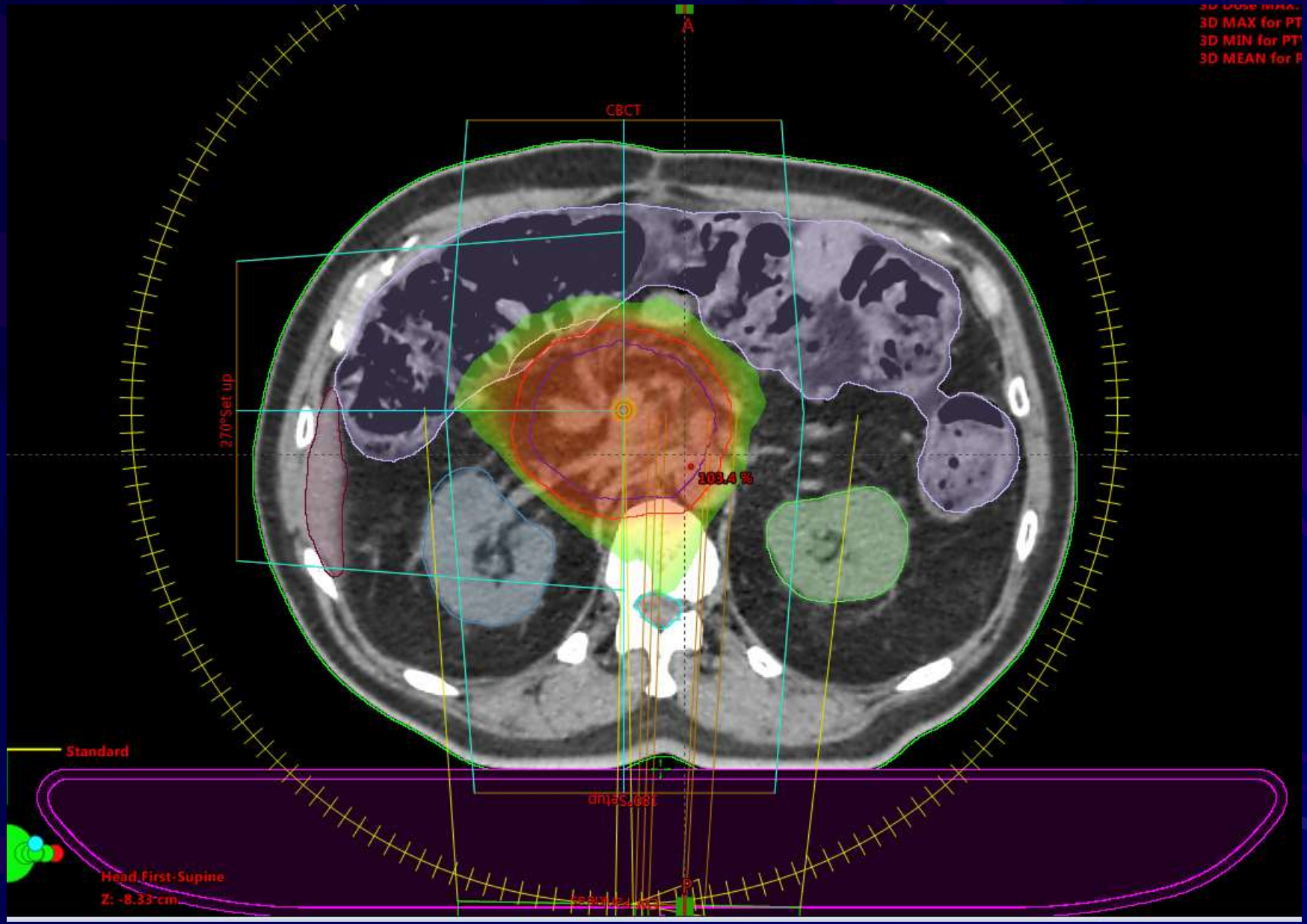

3D Dose MAX: 106.3 %
3D MAX for PTV Pankreas: 106.
3D MIN for PTV Pankreas: 85.9
3D MEAN for PTV Pankreas: 10
A
106.3 %
Standard
Head First-Supine
P


File Edit View Measure Structure 4D Tools
Selection Contouring Image Registration External Beam Planning Brachytherapy Planning Brachytherapy 2D Entry Plan Evaluation
Transversal
WB 68-Ga PSM - 30.12.2016 10:10
REGISTRATION
CT Image
PET Image
PET WB 68-Ga PSM
CBCT
Sagittal
WB 68-Ga PSM - 30.12.2016 10:10
Front
WB 68-Ga PSM - 30.12.2016 10:10
Standard, HFS
100 %

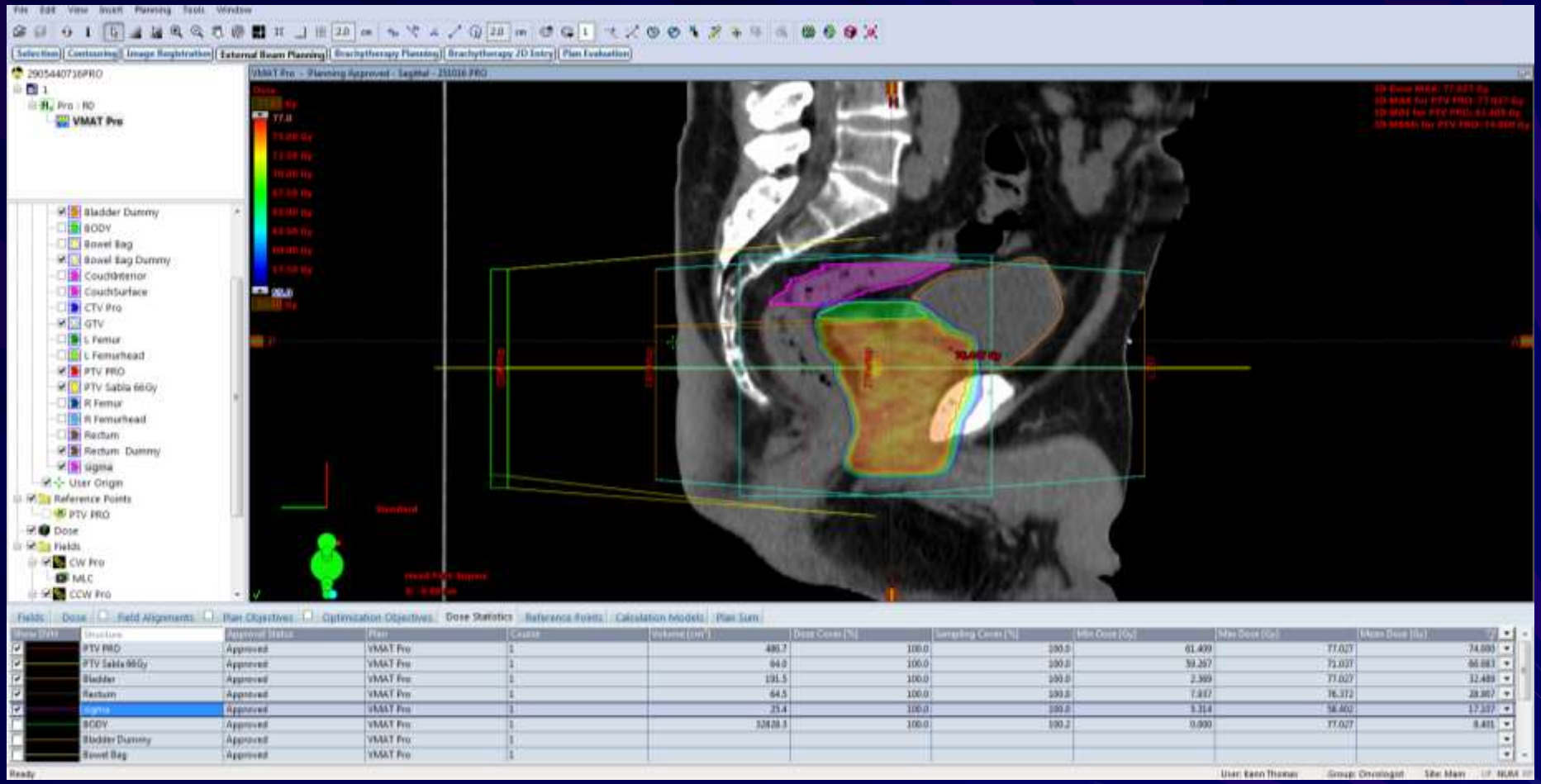



Transversal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
Isocenter: Treatment (Field: CW Pankreas - 03.02.2017 08:19:23)
A
R
L
P
20.0 cm
Standard, HFS
0 %
(Cerveny Maria
wienkav\kfjirocer 03.02.2017 08:59)
Sagittal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
P
A
F
20.0 cm
X: 0.09 cm
0 %
Frontal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
R
L
F
20.0 cm
Y: -13.35 cm
0 %


Transversal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
Isocenter: Treatment (Field: CW Pankreas - 03.02.2017 08:19:23)
A
R
L
P
20.0 cm
Standard, HFS
Z: -5.95 cm
(Cerveny Maria
wienkav\kfjrocer 03.02.2017 08:59)
100 %
Sagittal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
P
A
F
20.0 cm
X: 0.09 cm
100 %
Frontal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
R
L
F
20.0 cm
Y: -13.35 cm
100 %


A
3D MAX for PT
3D MIN for PT
3D MEAN for P
CBCT
270°Set up
103.4 %
180°Set up
Standard
Head First-Supine
Z: -8.33 cm
P


Dosismaximum in Sigma
67,6Gy!!



Lösung: SIS (simultan integriertes Sparing) der cranialen Region (Dmean 66Gy)
Dosismax. in Sigmaschlinge jetzt 58 Gy

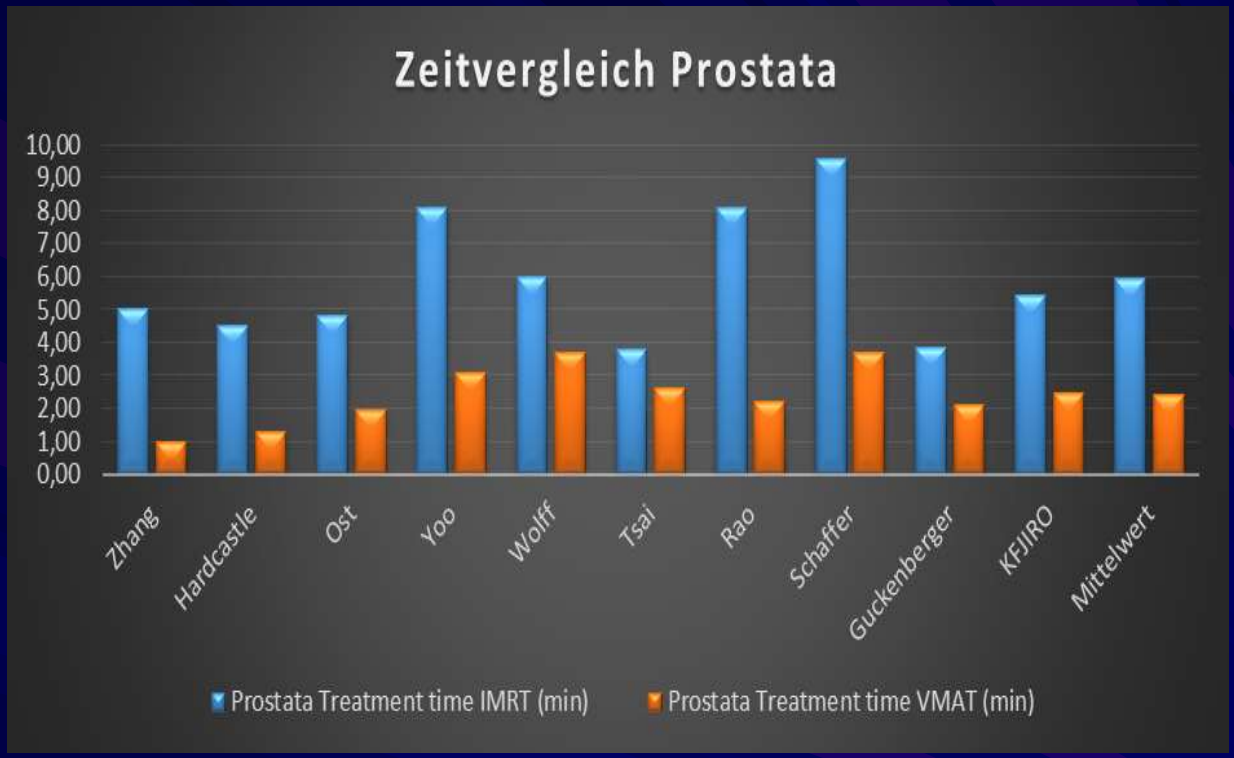
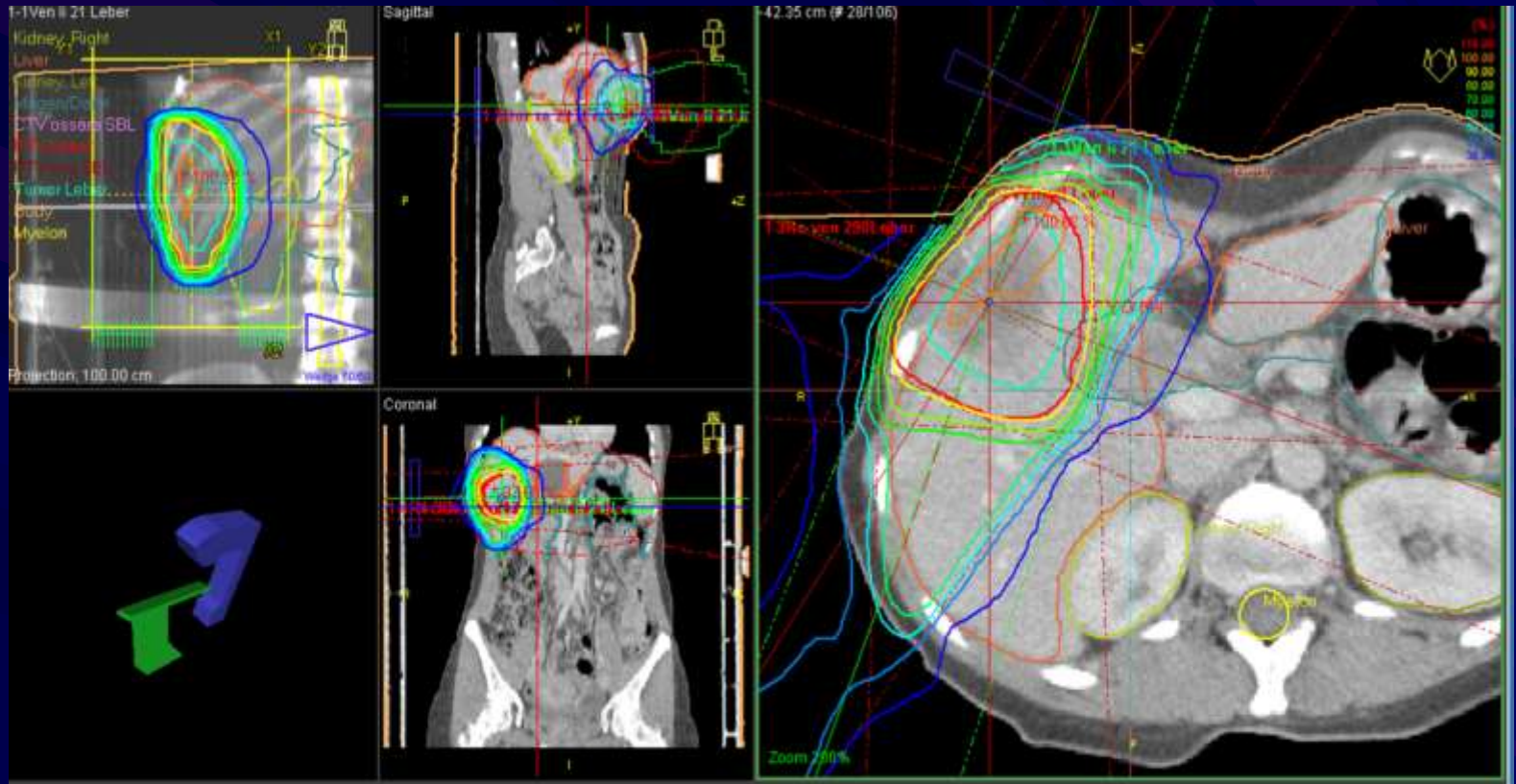


Abbildung 19: Auswertung IMRT & VMAT Zeitvergleich Prostata
Quelle British Journal of Radiology/SMZ Süd KFJIRO eigene Darstellungen

SBRT liver – 4th place of possibilities



Label	Unit	Energy	FX (cm)	X1 (cm)	X2 (cm)	FY (cm)	Y1 (cm)	Y2 (cm)	X (cm)	Y (cm)	Z (cm)	Y Offset (cm)	Depth (cm)	SSD (cm)	Gantry (deg)	Arc Dir	Collimator (deg)	Couch (deg)	Wedge
1-1Ve	BM_SYNERI	10.00 MV	<13.15>	<-6.36>	< 6.79>	< 7.20>	<-3.20>	< 4.00>	-6.79	-41.15	26.56	1.20	5.69	94.31	21.00	N/A	270.00	0.00	Wed
1-2Ve	BM_SYNERI	10.00 MV	< 7.26>	<-3.74>	< 3.52>	<13.20>	<-6.80>	< 6.40>	-6.79	-41.15	26.56	1.20	3.88	96.12	0.00	N/A	0.00	0.00	N/A
1-3R	BM_SYNERI	10.00 MV	< 7.70>	<-3.74>	< 3.96>	<13.20>	<-6.80>	< 6.40>	-6.79	-41.15	26.56	1.20	8.07	91.93	290.00	N/A	0.00	0.00	N/A
1-4R	BM_SYNERI	10.00 MV	< 8.00>	<-4.16>	< 3.84>	<13.20>	<-6.80>	< 6.40>	-6.79	-41.15	26.56	1.20	15.64	84.36	270.00	N/A	0.00	0.00	N/A
1-5D	BM_SYNERI	10.00 MV	<13.26>	<-6.84>	< 6.42>	< 7.20>	<-2.80>	< 4.40>	-6.79	-41.15	26.56	1.20	20.44	79.56	213.00	N/A	90.00	0.00	Wed

Neoadjuvante CRT

Stabilerer Performancestatus präoperativ

Tumorcontouring

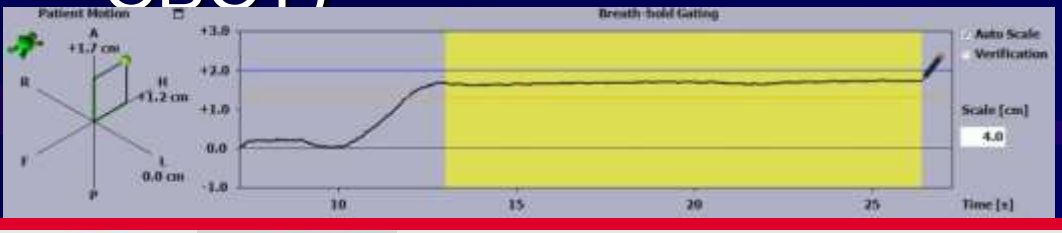
Sauerstoffeffekt

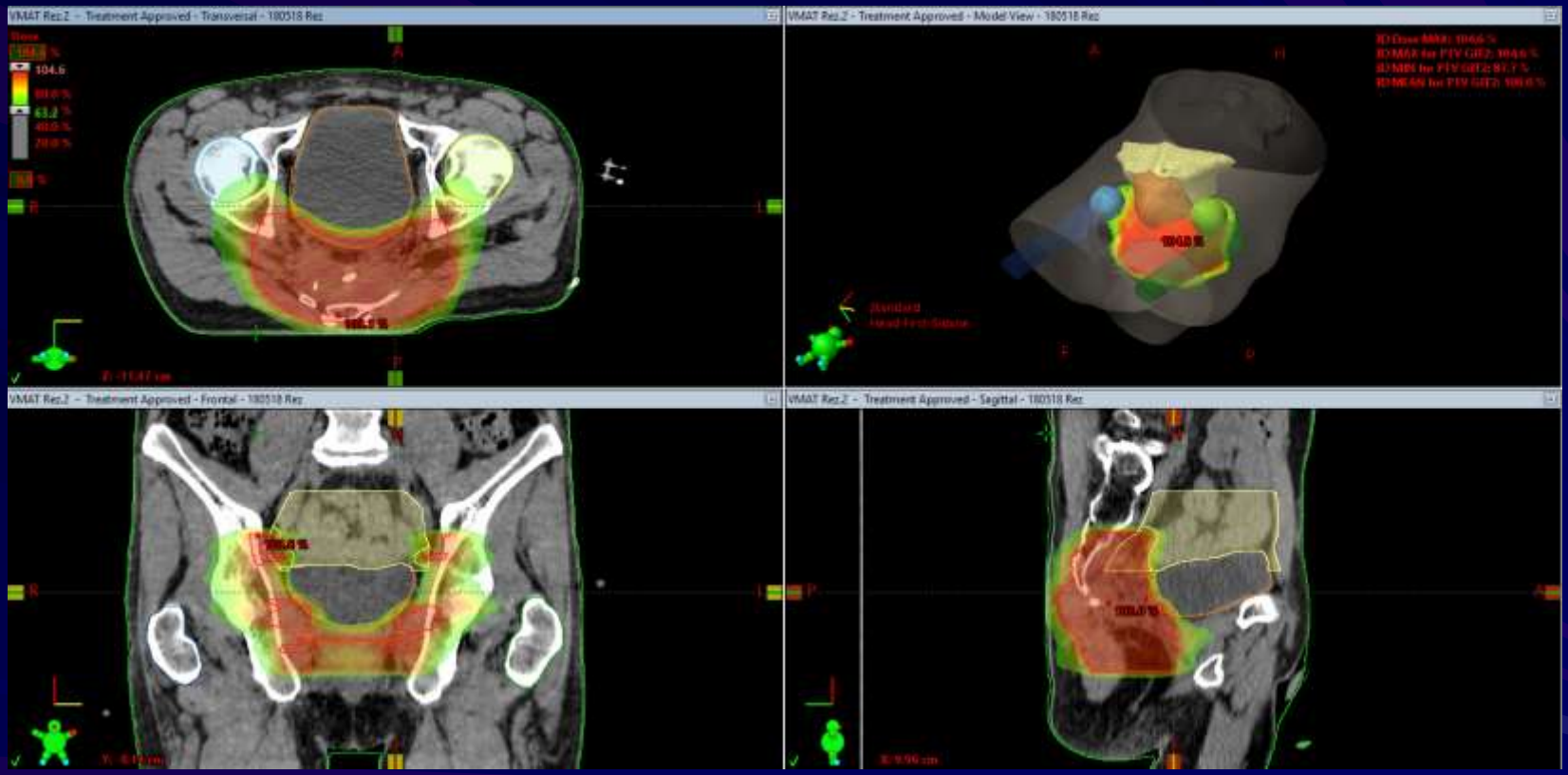
Keine p.op.Darmfixierung

Accelerierte Dosierung

moderate Stereotaxie?

Neue Technologie (VMAT, Atemgating, CBCT)




VMAT Rez.2 – Treatment Approved - Transversal - 180518 Rez
VMAT Rez.2 – Treatment Approved - Model View - 180518 Rez
VMAT Rez.2 – Treatment Approved - Frontal - 180518 Rez
VMAT Rez.2 – Treatment Approved - Sagittal - 180518 Rez

Intraoperative Radiotherapie

PRÄVENTION

Structural stability of human fibroblast growth factor-1 is essential for protective effects against radiation-induced intestinal damage.

Nakayama F et al
IIJROBP 2013;85:477-83

Effect of antioxidant supplementation on digestive enzymes in radiation induced intestinal damage in rats

Anwar M et al
IJROBP2013,89(12):1061-70

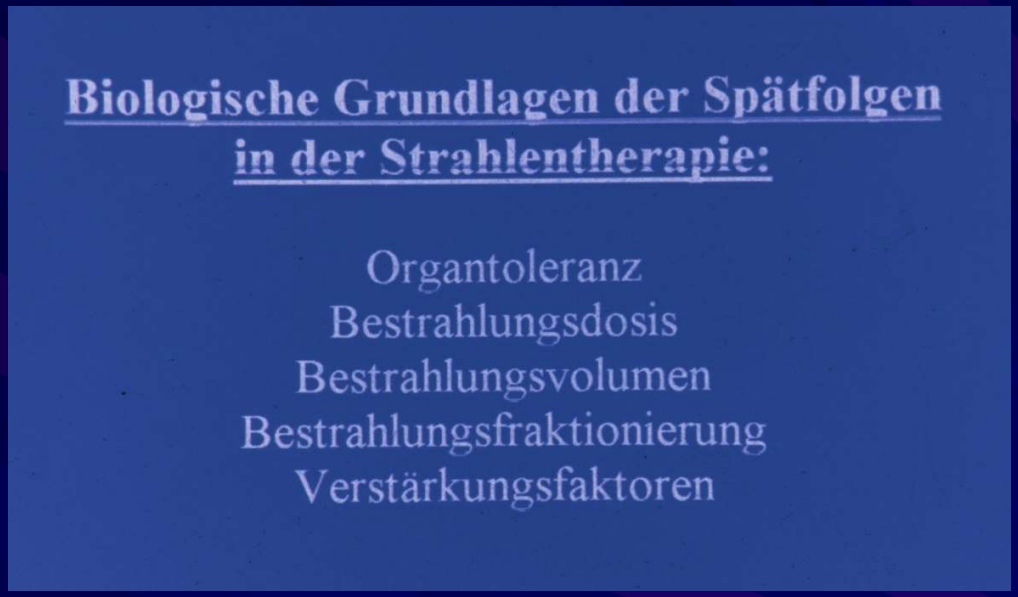
Amifostine alleviates radiation-induced lethal small bowel damage via promotion of 14-3-mediated nuclear p53 accumulation

Eng-Yen Huang et al
Oncotarget.2014;5(20):9756-69

A Novel Mouse Model to Study Image-Guided, Radiation-Induced Intestinal Injury andPreclinical Screening of Radioprotectors

I Verginadis et al
Mol and cellular Pathobiology 2017

PRÄVENTION

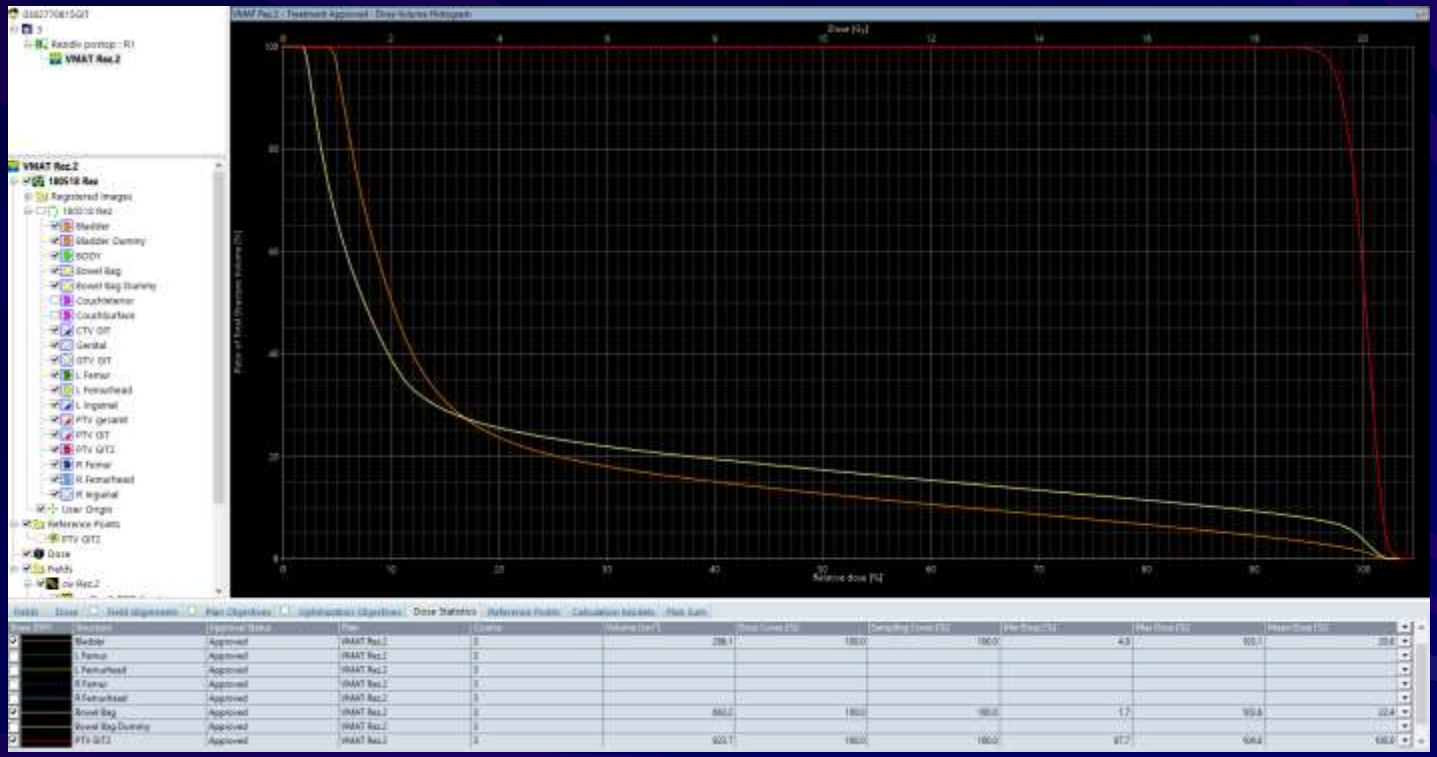


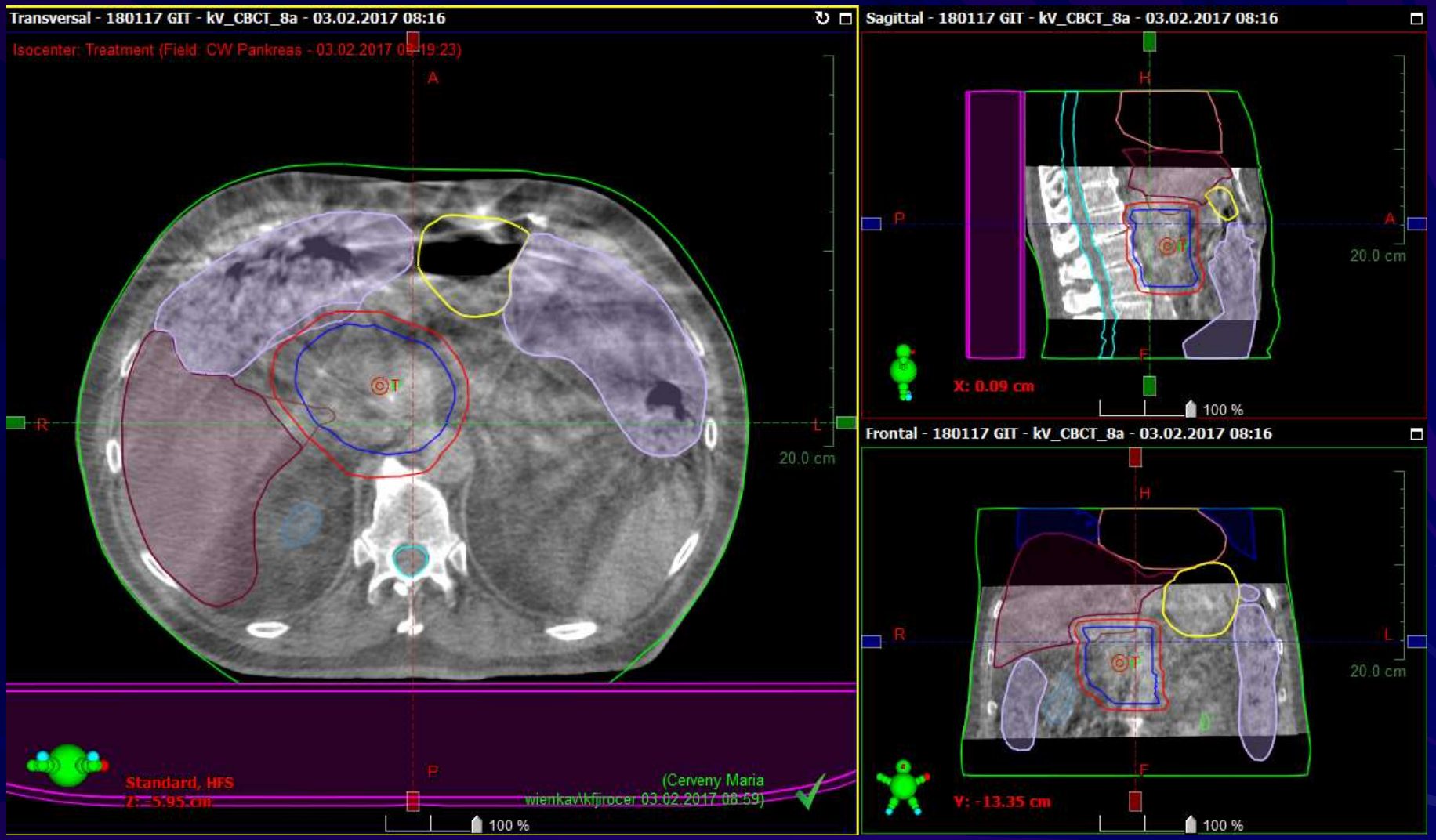
Planung nach Quanteckriterien

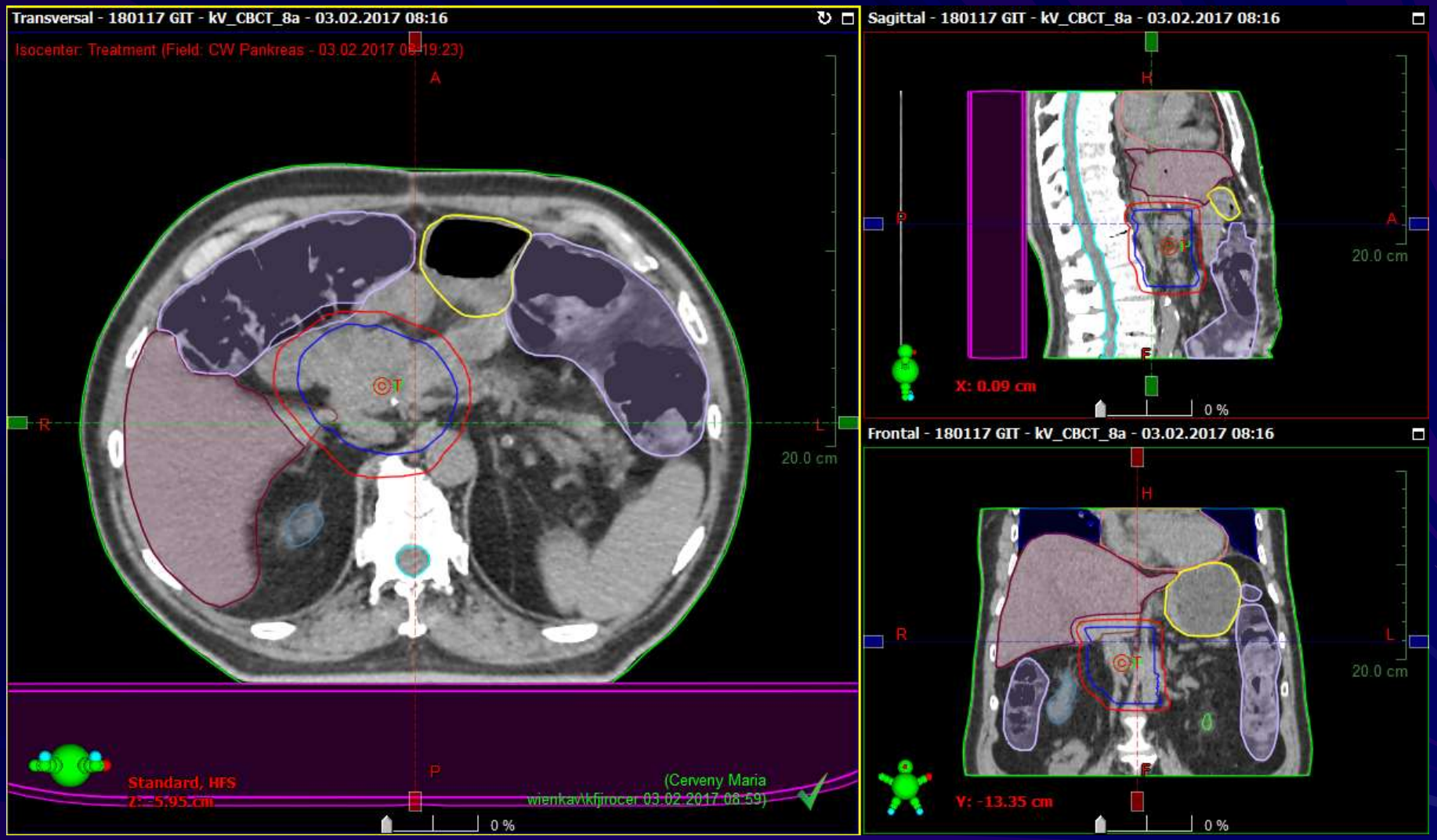
Bestrahlungsvolumen so gering wie möglich

VMAT und tägl. CBCT

THE HUMAN FACTOR ...




Transversal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
Isocenter: Treatment (Field: CW Pankreas - 03.02.2017 08:19:23)
A
R
L
P
20.0 cm
Standard, HFS
Z: -5.95 cm
100 %
(Cerveny Maria
wienkav\kfjrocer 03.02.2017 08:59)
Sagittal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
P
A
F
20.0 cm
X: 0.09 cm
100 %
Frontal - 180117 GIT - kV_CBCT_8a - 03.02.2017 08:16
H
R
L
F
20.0 cm
Y: -13.35 cm
100 %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Isocenter: Treatment (Field: CW Pankreas - 03.02.2017 08:19:23)
A
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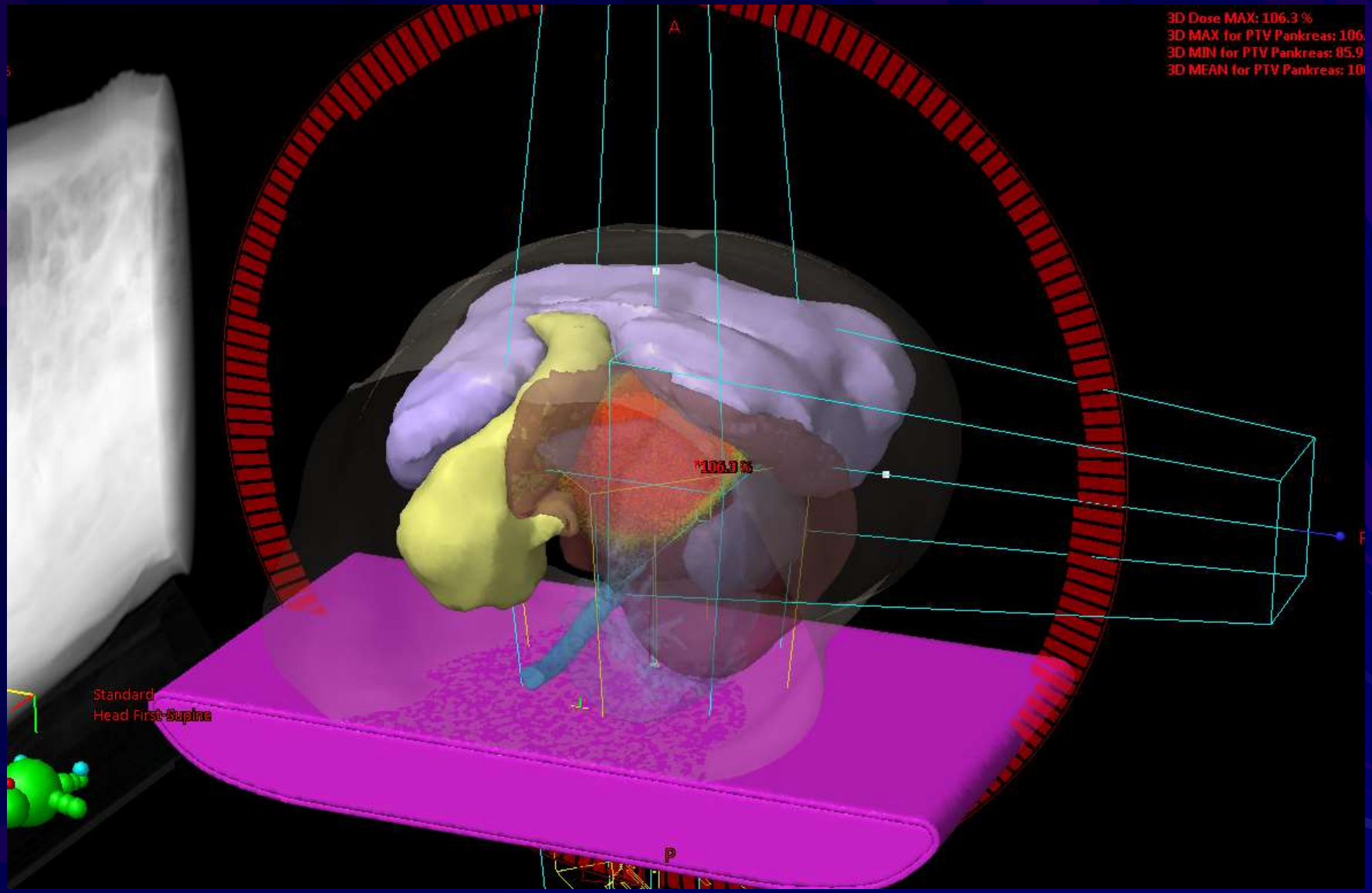
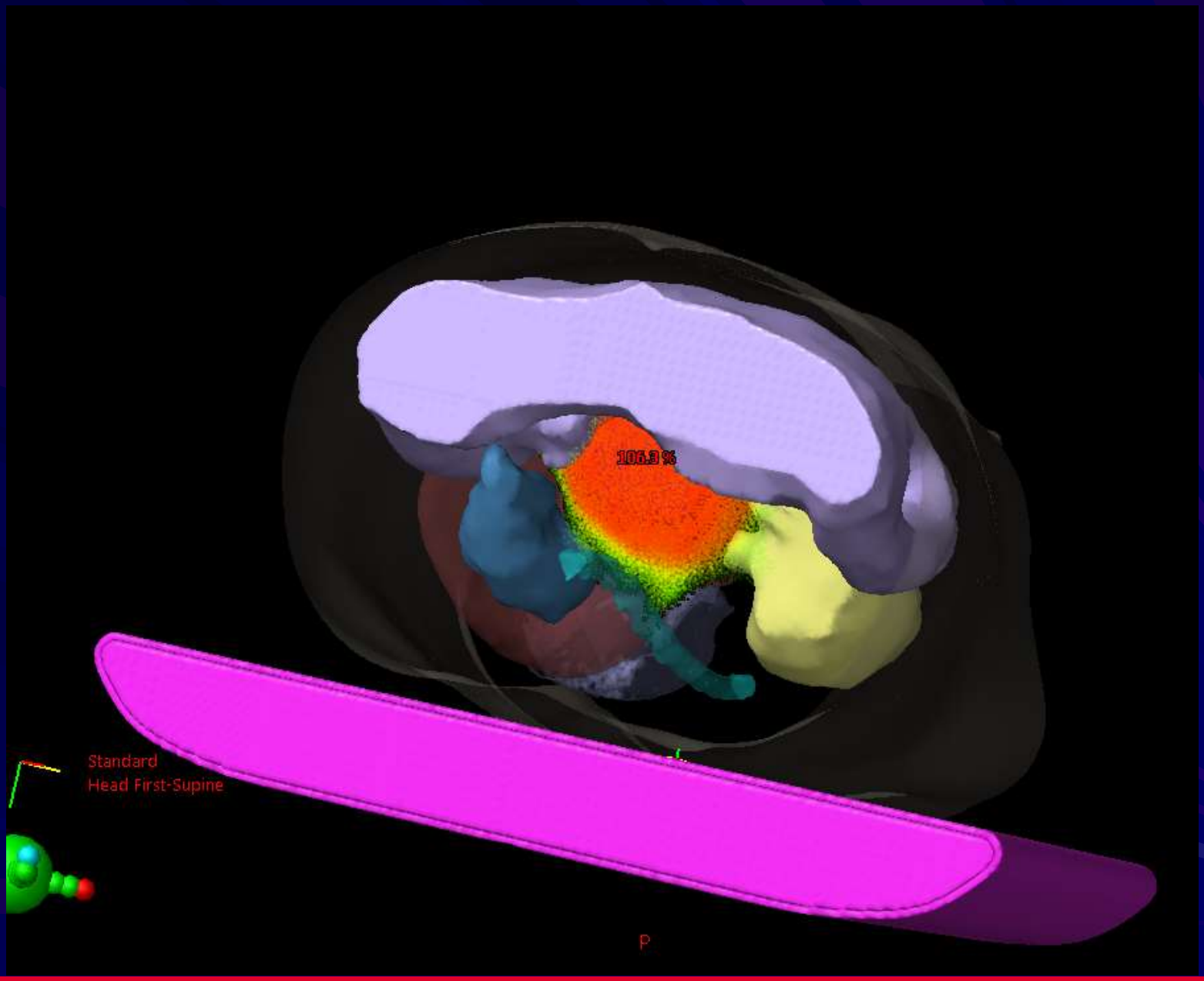
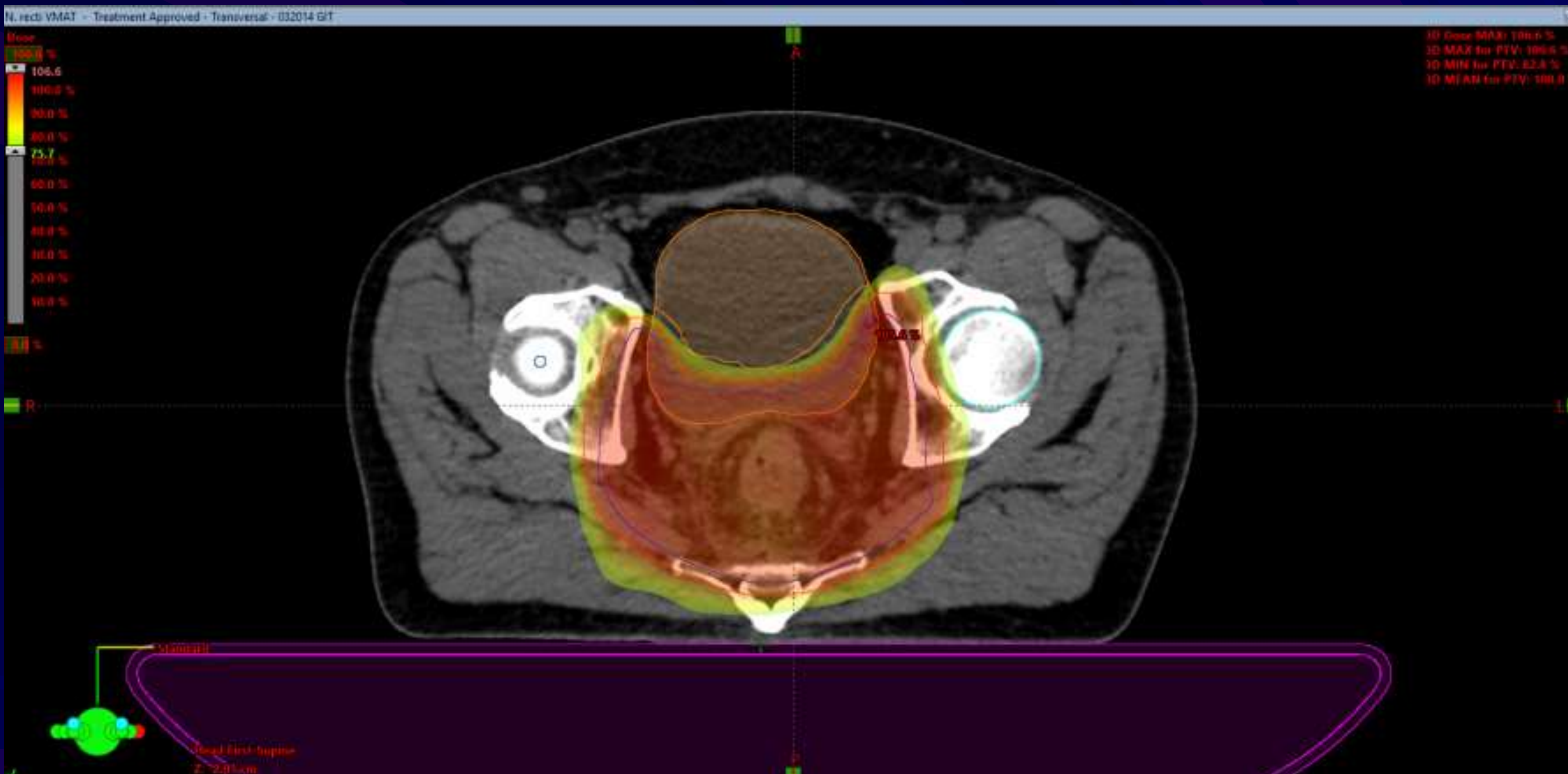
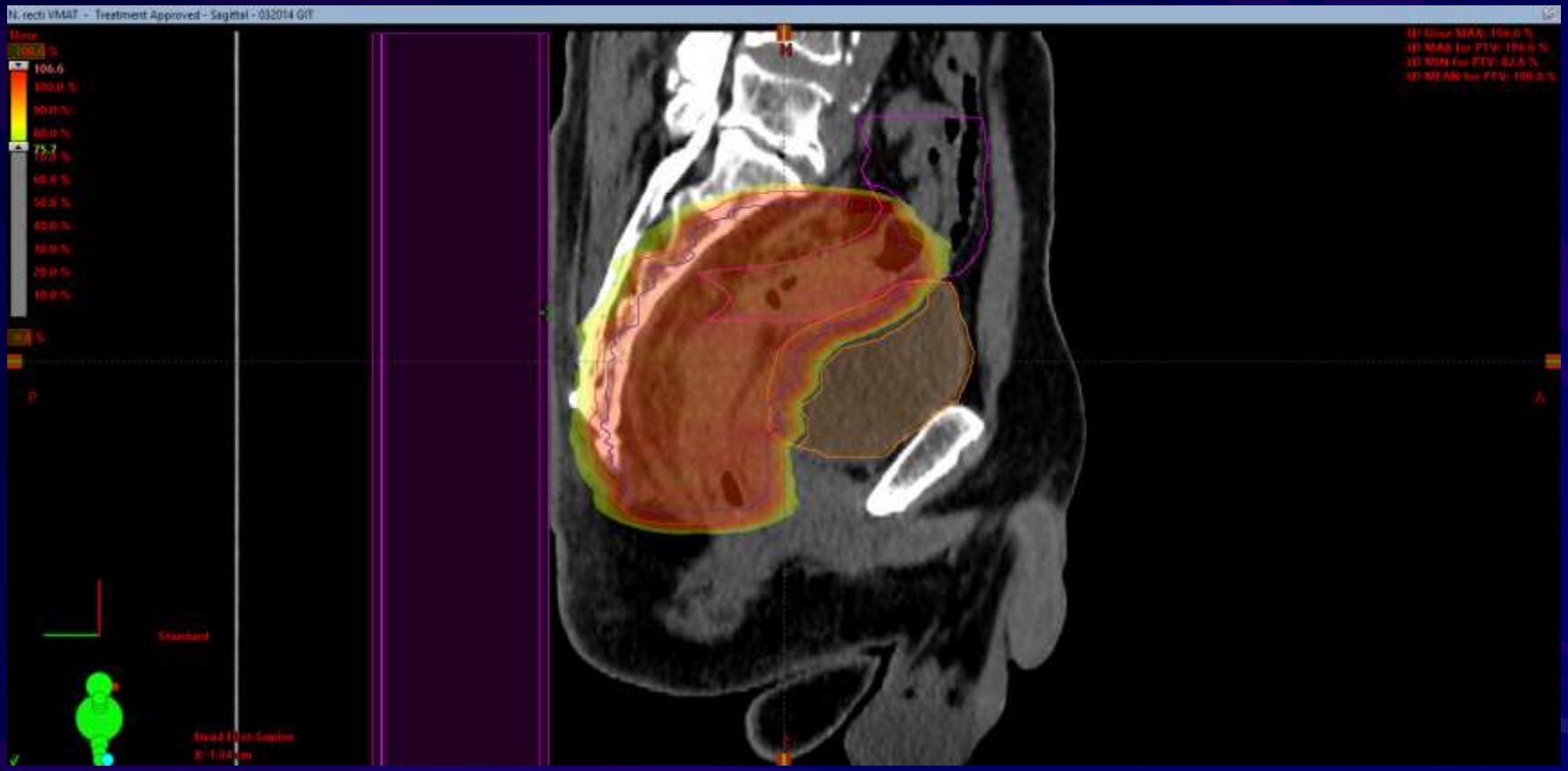
H
R
L
F
20.0 cm
Y: -13.35 cm
0 %


3D Dose MAX: 106.3 %
3D MAX for PTV Pankreas: 106.
3D MIN for PTV Pankreas: 85.9
3D MEAN for PTV Pankreas: 10
A
106.3 %
Standard
Head First-Supine
P


106.3 %
Standard
Head First-Supine
P


N. recti VMAT - Treatment Approved - Transversal - 032014 GIT
106.6
75.7


N. recti VMAT - Treatment Approved - Sagittal - 032014 GIT
106.6
75.7
Standard

Effect of antioxidant supplementation on digestive enzymes in radiation induced intestinal damage in rats.

Anwar M[1], Nanda N, Bhatia A, Akhtar R, Mahmood S.

AUTHOR INFORMATION

[1]

Department of Experimental Medicine & Biotechnology, Postgraduate Institute of Medical Education & Research , Chandigarh , India.

Abstract

Chandigarh , India.

Abstract

PURPOSE:

Intestinal mucosa, a rapidly proliferating tissue, is highly sensitive to radiation and undergoes apoptosis as a consequence of over generation of oxidative free radicals and the lack of the antioxidants. Thus the present study was designed to investigate the intestinal damage induced by radiation and to study if supplementation of the diet with antioxidant vitamins could ameliorate the intestinal damage and its digestive activity, as determined by the expression of various border enzymes.

MATERIALS AND METHODS:

Swiss Albino rats (150-200 g body weight) were divided into six groups. Group I: Control untreated; Group II: Irradiated; Group III: Irradiated + vitamin A; Group IV: Irradiated + vitamin C; Group V: Irradiated + vitamin E; and Group VI: Irradiated + lycopene. Animals were exposed to whole body γ-radiation from (60)Co at the rate of 8 Gy for 15 min/rat. Intestinal morphology and changes in various digestive enzymes together with, DNA damage was studied in six groups and each group consisted of 18 animals.

RESULTS:

The gastrointestinal toxicity resulted in malabsorption, diarrhoea, weight loss, loss of appetite, abdominal haemorrhage and hair loss. The activities of sucrase and alkaline phosphatase were elevated and those of lactase, leucine aminopeptidase (LAP) and gamma-glutamyl transpeptidase or tranferase (γ-GTP) were markedly reduced. Antioxidant vitamin A, C or E supplementations prevented changes in brush border enzyme activities as compared to lycopene administration in rat intestine by radiation exposure. Intestinal histology showed that the vitamin supplementation to irradiated rats minimized the intestinal damage in rats.

CONCLUSION:

These findings suggest that the epithelial lining of the intestine is highly sensitive to radiation exposure and supplementation of antioxidant vitamins is helpful in minimizing the intestinal damage and supplementation by vitamin E was most potent in ameliorating the intestinal aberrations.

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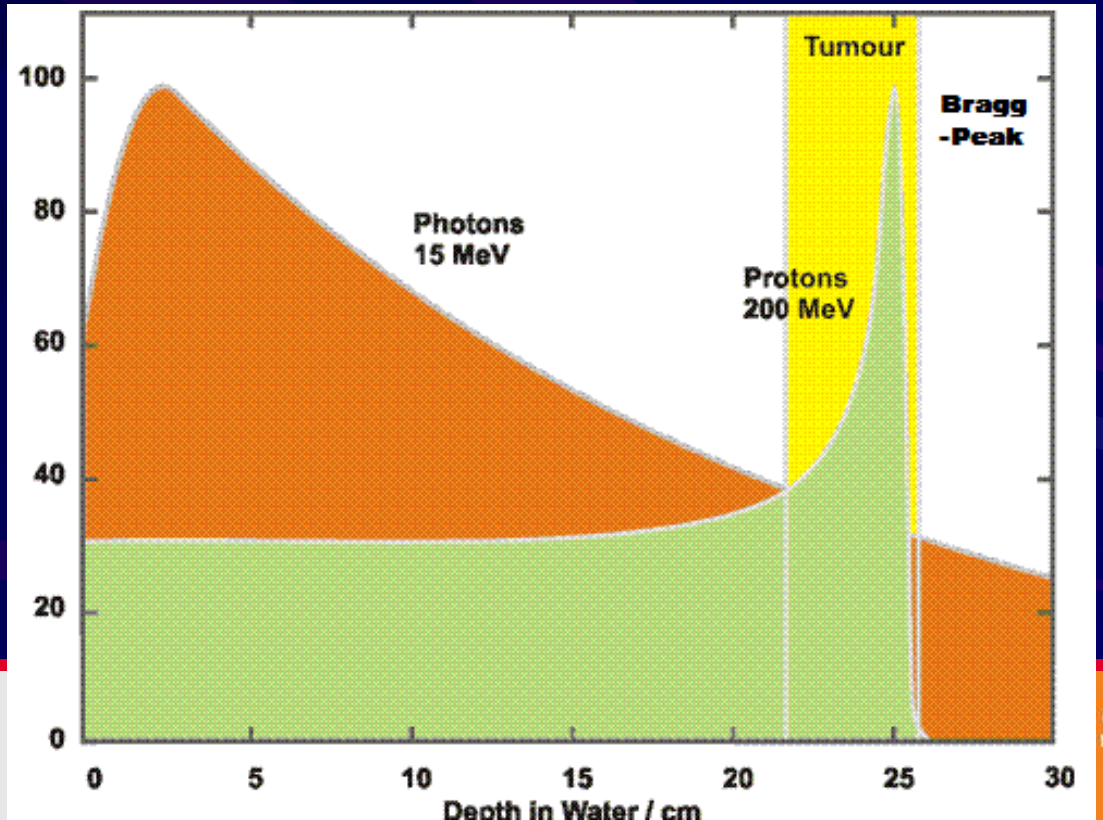


Structural stability of human fibroblast growth factor-1 is essential for protective effects against radiation**-induced intestinal** damage**.**

Nakayama F[1], Umeda S, Yasuda T, Asada M, Motomura K, Suzuki M, Zakrzewska M, Imamura T, Imai T.
AUTHOR INFORMATION
1
Advanced Radiation Biology Research Program, Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan. f_naka@nirs.go.jp

Abstract

PURPOSE:

Human fibroblast growth factor-1 (FGF1) has radioprotective effects on the intestine, although its structural instability limits its potential for practical use. Several stable FGF1 mutants were created increasing stability in the order, wild-type FGF1, single mutants (Q40P, S47I, and H93G), Q40P/S47I, and Q40P/S47I/H93G. This study evaluated the contribution of the structural stability of FGF1 to its radioprotective effect.

METHODS AND MATERIALS:

Each FGF1 mutant was administered intraperitoneally to BALB/c mice in the absence of heparin 24 h before or after total body irradiation (TBI) with γ-rays at 8-12 Gy. Several radioprotective effects were examined in the jejunum.

RESULTS:

Q40P/S47I/H93G could activate all subtypes of FGF receptors in vitro much more strongly than the wild-type without endogenous or exogenous heparin. Preirradiation treatment with Q40P/S47I/H93G significantly increased crypt survival more than wild-type FGF1 after TBI at 10 or 12 Gy, and postirradiation treatment with Q40P/S47I/H93G was effective in promoting crypt survival after TBI at 10, 11, or 12 Gy. In addition, crypt cell proliferation, crypt depth, and epithelial differentiation were significantly promoted by postirradiation treatment with Q40P/S47I/H93G. The level of stability of FGF1 mutants correlated with their mitogenic activities in vitro in the absence of heparin; however, preirradiation treatment with the mutants increased the crypt number to almost the same level as Q40P/S47I/H93G. When given 24 h after TBI at 10 Gy, all FGF1 mutants increased crypt survival more than wild-type FGF1, and Q40P/S47I/H93G had the strongest mitogenic effects in intestinal epithelial cells after radiation damage. Moreover, Q40P/S47I/H93G prolonged mouse survival after TBI because of the repair of intestinal damage.

CONCLUSION:

These findings suggest that the structural stability of FGF1 can contribute to the enhancement of protective effects against radiation-induced intestinal damage. Therefore, Q40P/S47I/H93G is pharmacologically one of the most promising candidates for clinical applications for radiation-induced gastrointestinal syndrome.

Locally Advanced, Unresectable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline

Edward P. Balaban et al

To provide evidence-based recommendations to oncologists and others for treatment of patients with locally advanced, unresectable pancreatic cancer.

Methods

American Society of Clinical Oncology convened an Expert Panel of medical oncology, radiation oncology, surgical oncology, gastroenterology, palliative care, and advocacy experts and conducted a systematic review of the literature from January 2002 to June 2015. Outcomes included overall survival, disease-free survival, progression-free survival, and adverse events.

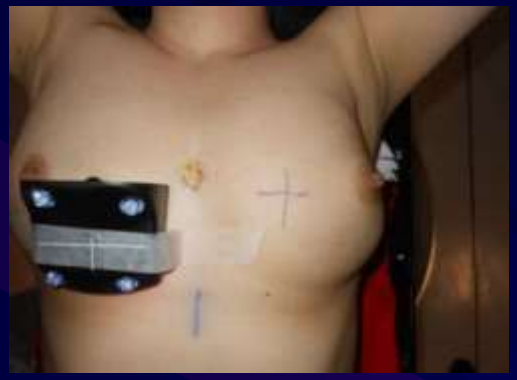
Results

Twenty-six randomized controlled trials met the systematic review criteria.

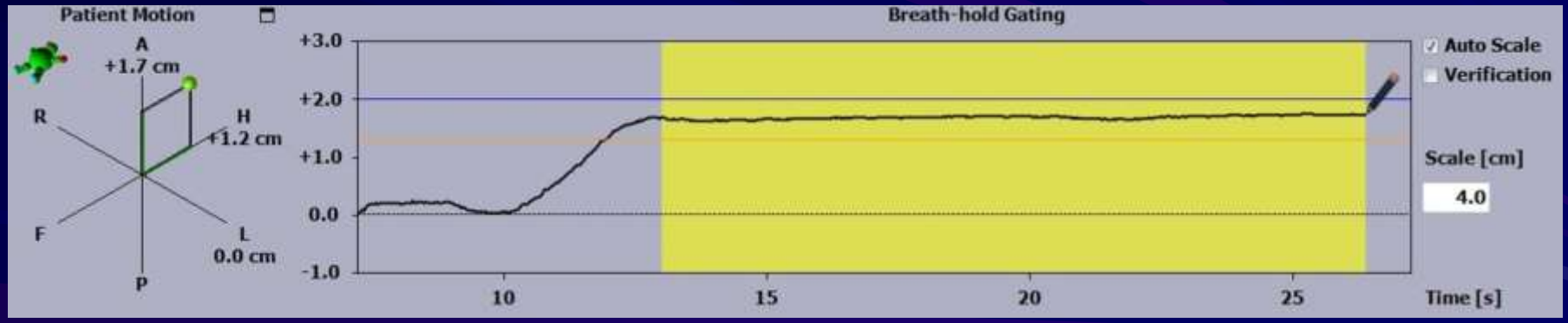
Recommendations

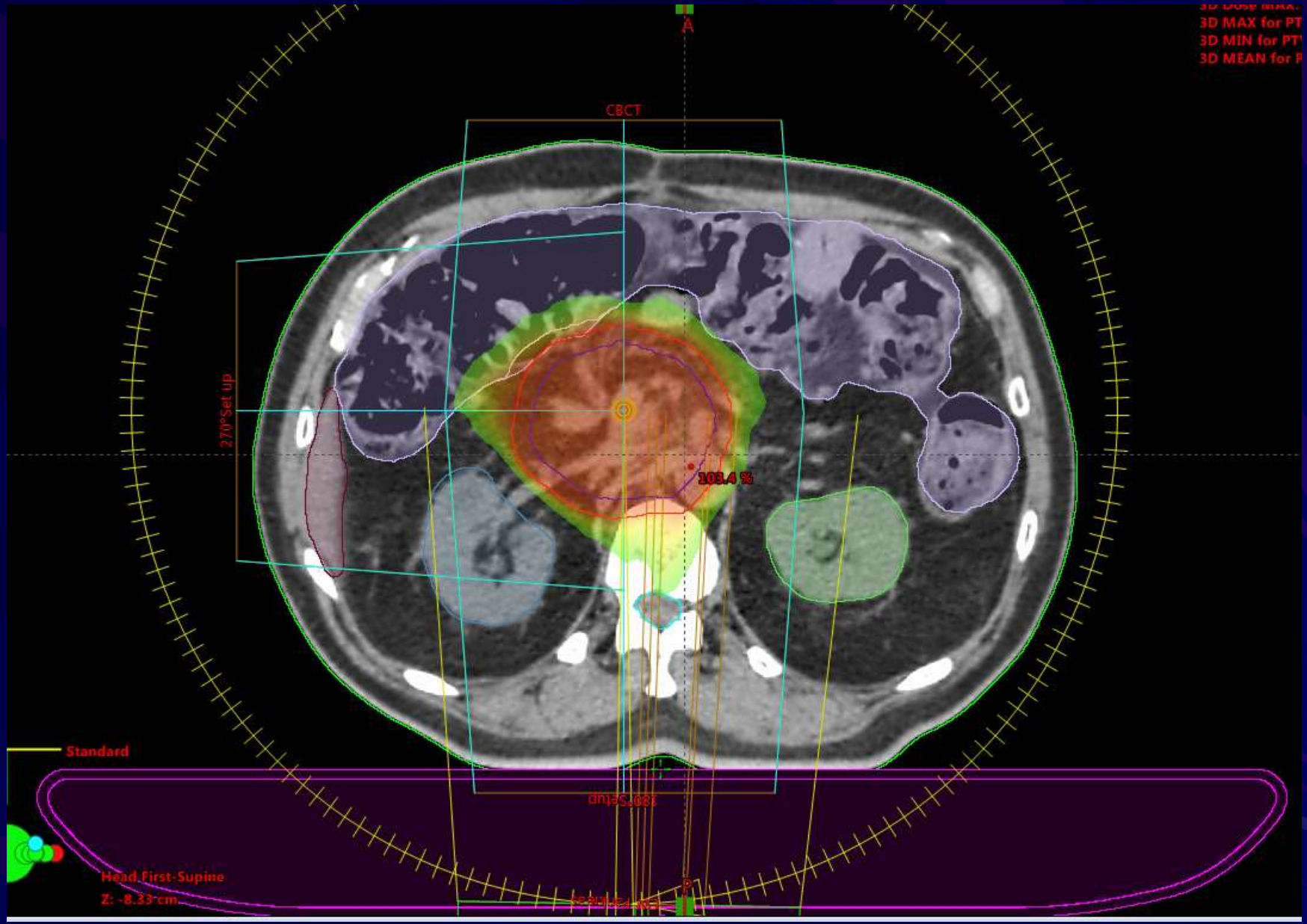
A multiphase computed tomography scan of the chest, abdomen, and pelvis should be performed. Baseline performance status and comorbidity profile should be evaluated. The goals of care, patient preferences, psychological status, support systems, and symptoms should guide decisions for treatments. A palliative care referral should occur at first visit. Initial systemic chemotherapy (6months)with a combination regimen is recommended for most patients (for some patients radiation therapy may be offered up front) with Eastern Cooperative Oncology Group performance status 0 or 1 and a favorable comorbidity profile. There is no clear evidence to support one regimen over another. The gemcitabinebased combinations and treatments recommended in themetastatic setting (eg, fluorouracil, leucovorin, irinotecan, and oxaliplatin and gemcitabine plus nanoparticle albumin-bound paclitaxel) have not been evaluated in randomized controlled trials involving locally advanced, unresectable pancreatic cancer. If there is local disease progression after induction chemotherapy, without metastasis, then radiation therapy or stereotactic body radiotherapy may be offered also with an Eastern Cooperative Oncology Group performance status#2 and an adequate comorbidity profile. If there is stable disease after 6 months of induction chemotherapy but unacceptable toxicities, radiation therapy may be offered as an alternative. Patients with disease progression should be offered treatment per the ASCO Metastatic Pancreatic Cancer Treatment Guideline. Follow-up visits every 3 to 4months are recommended. Additional information is available at www.asco.org/guidelines/LAPC and www.asco.org/guidelines/MetPC and www.asco.org/guidelineswiki.

J Clin Oncol 34:2654-2668.



Example of a breathing curve




A
3D MAX for PT
3D MIN for PT
3D MEAN for P
CBCT
270°Set up
103.4 %
Standard
Head First-Supine
Z: -8.33 cm
P

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