

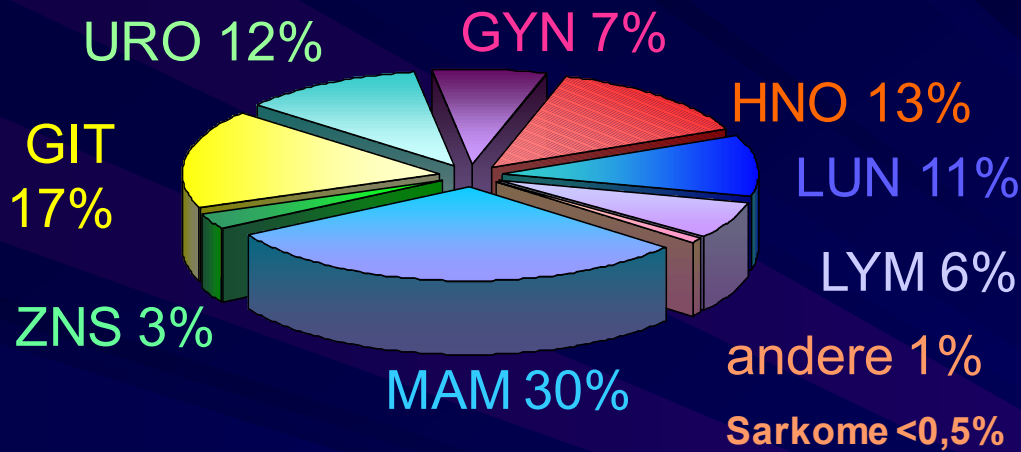
Neoadjuvante Radiotherapie – Vollremission bis Langzeitschaden

Prim. Univ.-Doz. Dr. A.U. Schratter-Sehn

14. Juni 2016

17. Frühjahrstagung der I.S.D.S.
Brac, Kroatien

Statistik @ IRO-KFJ/SMZ-Süd



Pat.:RST,,HANUSCH, Priv.KH

- ca 1500 neue Pat./Jahr
- 100 Pat./Tag an
2 Linearbeschleuniger
- V-MAT, Stereotaxie

3D-4D-Planung:

- Min. 4
Pläne/Patient
- Atemgating

IGRT

- KV- Einstellfelder
- MV-Feldaufnahmen
während
Bestrahlung
- CBCT

Moderne Radiotherapie

Teletherapie

Konformale RT

IMRT (IntensitätsModulierte RT)

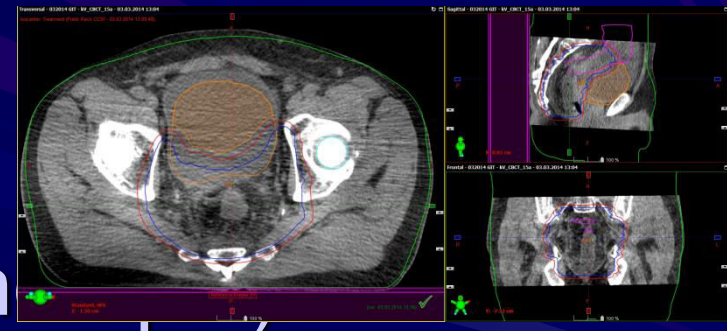
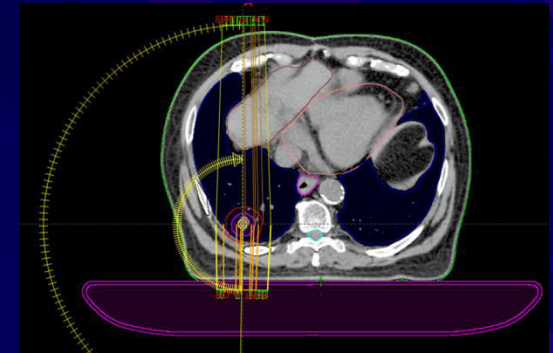
V-MAT (Volumetric Modulated Arc Therapie)

Stereotaxie

SIB-IMRT (Simultan Integrierter Boost)

IGRT (Image-guided radiation therapy)

IORT (Intra Operative RadioTh



Atemgating

Neoadjuvante Radiotherapie – Vollremission bis Langzeitschaden

- Warum präoperativ?
- Langzeit oder Kurzzeitvorbestrahlung?
- Minimierung der Spätfolgen?
- Optimales Intervall zw RT und OP?
- ASCO 2016?
- Wait and Watch od. trans-anale Excision?
- Protonen?

Warum PRÄOPERATIVE RADIOTHERAPIE

■ Strahlenbiologische Vorteile

Blut-O₂-Versorgung, höhere Chemokonzentration

■ Keine allfällige postop. Fixation

Dünndarm-Blasenschonung

■ Zelldevitalisierung u. Tu-Regression

■ Downstaging-Downsizing

■ Spinktererhalt

■ Rezidivsenkung



Langzeit oder Kurzzeitvorbestrahlung?

Langzeitvorbestrahlung

25-28x1.8 GY +CHT

- T3/T4 od.N+ Tumore
- Downstaging, Downsizing
lokal fortgeschrittene Tumore
- Tiefsitzende Tumoren
(Sphinktererhaltung)
- CHT Applikation
(Zytotoxizität,
Chemosensibilisierung)

Kurzzeitvorbestrahlung

5x5 Gy in 5d

- T2 N+, T3 Tumore
- Primäre Operabilität TME
- Tumoren mind. 6 cm ab ano
Sphinkter, Perineum nicht includ.
- Zelldevitalisierung
- Multimorbide, höchstbetagte Pat.
- Chemotherapie nicht möglich

Minimierung der Strahlenfolgen

Acutreaktionen

Rektum: 5% Wundheilungsstörungen im Anastomosenbereich (passagere Colostomie), kein Neorektumpouch (Stuhlkapazitätnormalisierung nach 6 Monaten)

Blase: Zystitische Beschwerden, Blasenentleerungsstörung

Dünndarm: Diarrhoen

Spätfolgen

Rektum: Stenosen, Tenesmen, Multistuhlfrequenz, Schleimhautblutungen

Dünndarm: Fibrosierungen, Stenosierungen, Fistelbildungen, Ileus

Sphinkter: Fibrosierungen, Stenosen, Sphinkterschwäche (2% nach coloanal Anastomosen)

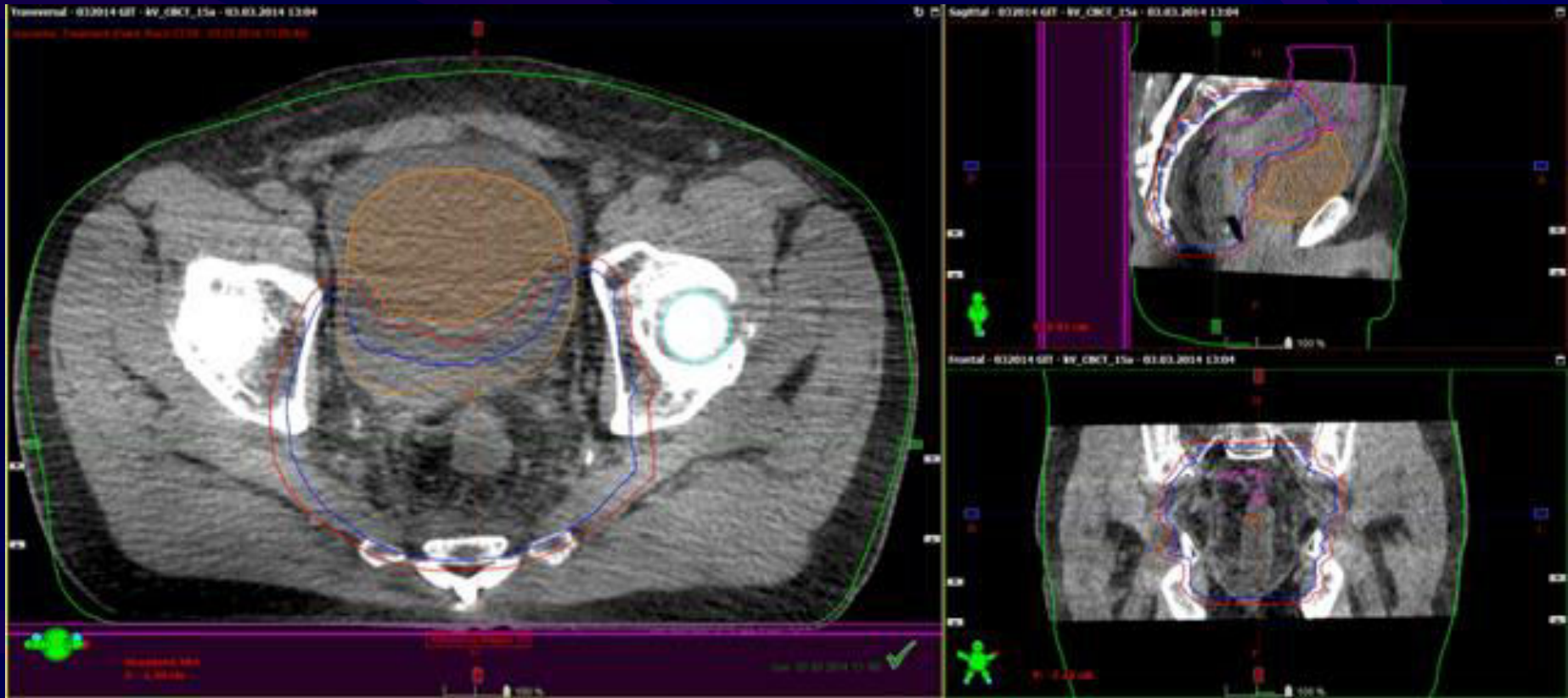
Blase: Schrumpfblase, Schleimhautblutungen

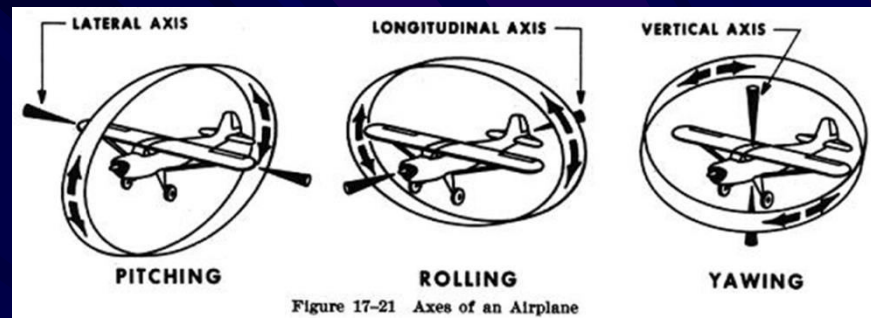
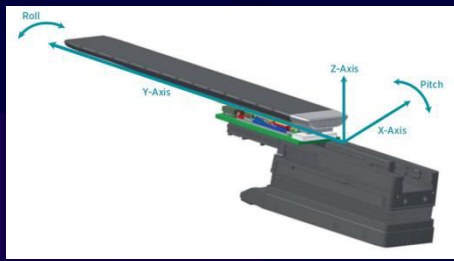
Sexualfunktion: Spätfolgen nach mehreren Jahren (erektiler Dysfunktion)

Minimierung der Strahlenfolgen?

- Volumeneinsparung!! Hochpräzisionsbestrahlung
V-MAT mit IGRT
- Bestrahlung immer mit voller Blase (ca.200ml)
- Dosisersparung
- Operation nach mind 7 Wochen
(bis Acutreaktionen abgeheilt)
- Pflegemaßnahmen

Matching CT mit CBCT

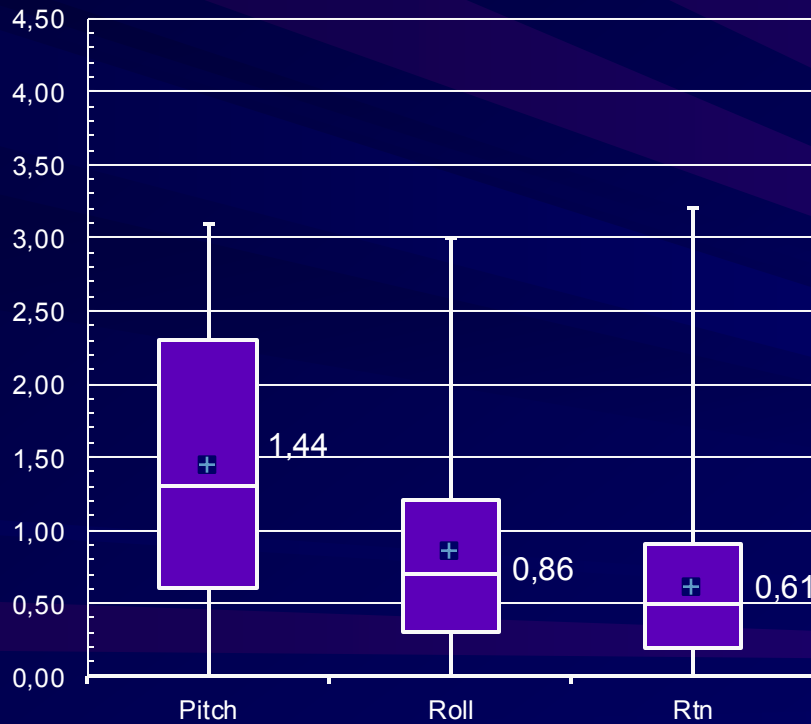




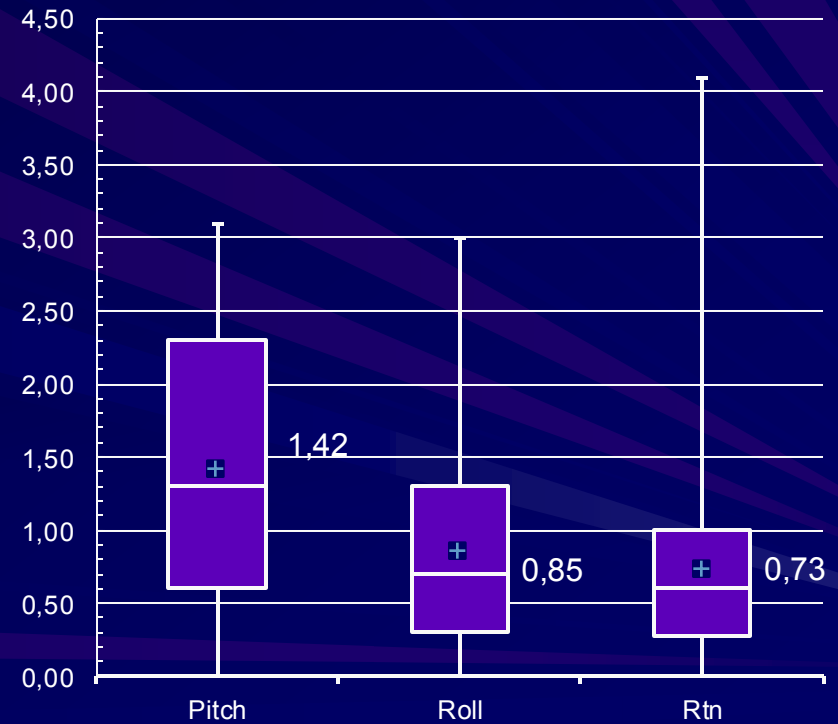
■ Prostata (n=1470)

■ Recti (n=761)

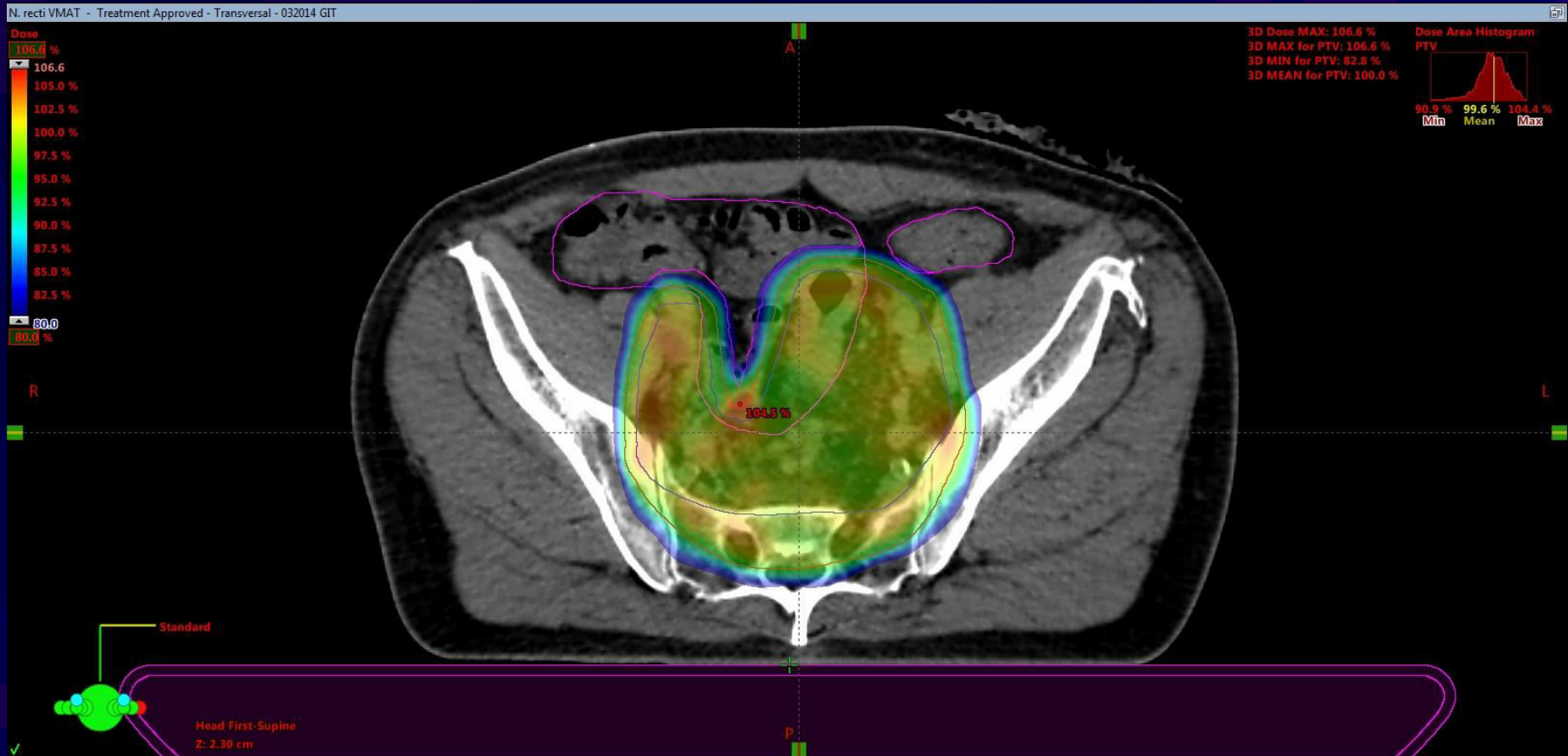
Rotationen [°]



Rotationen [°]



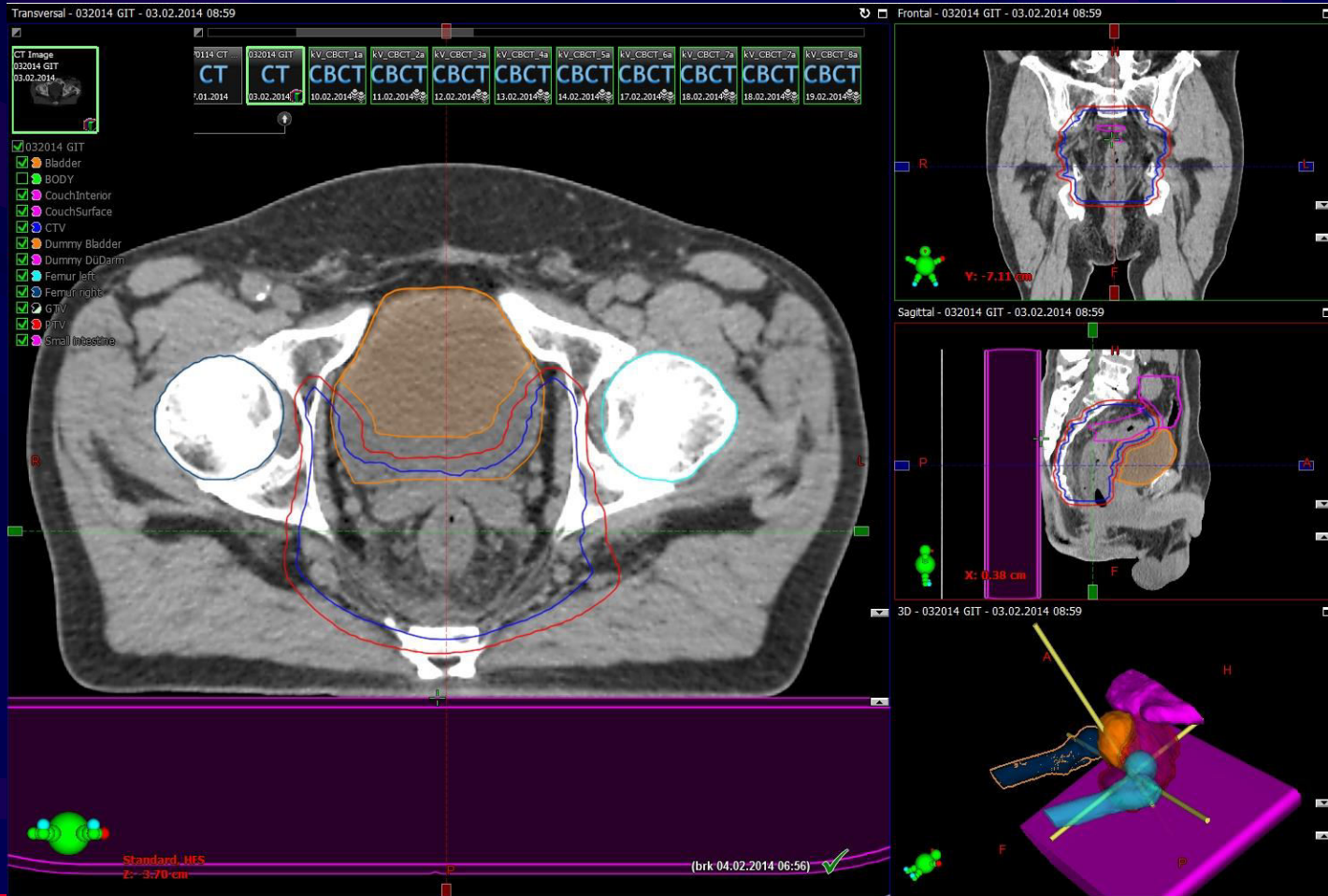
Dünndarmschonung



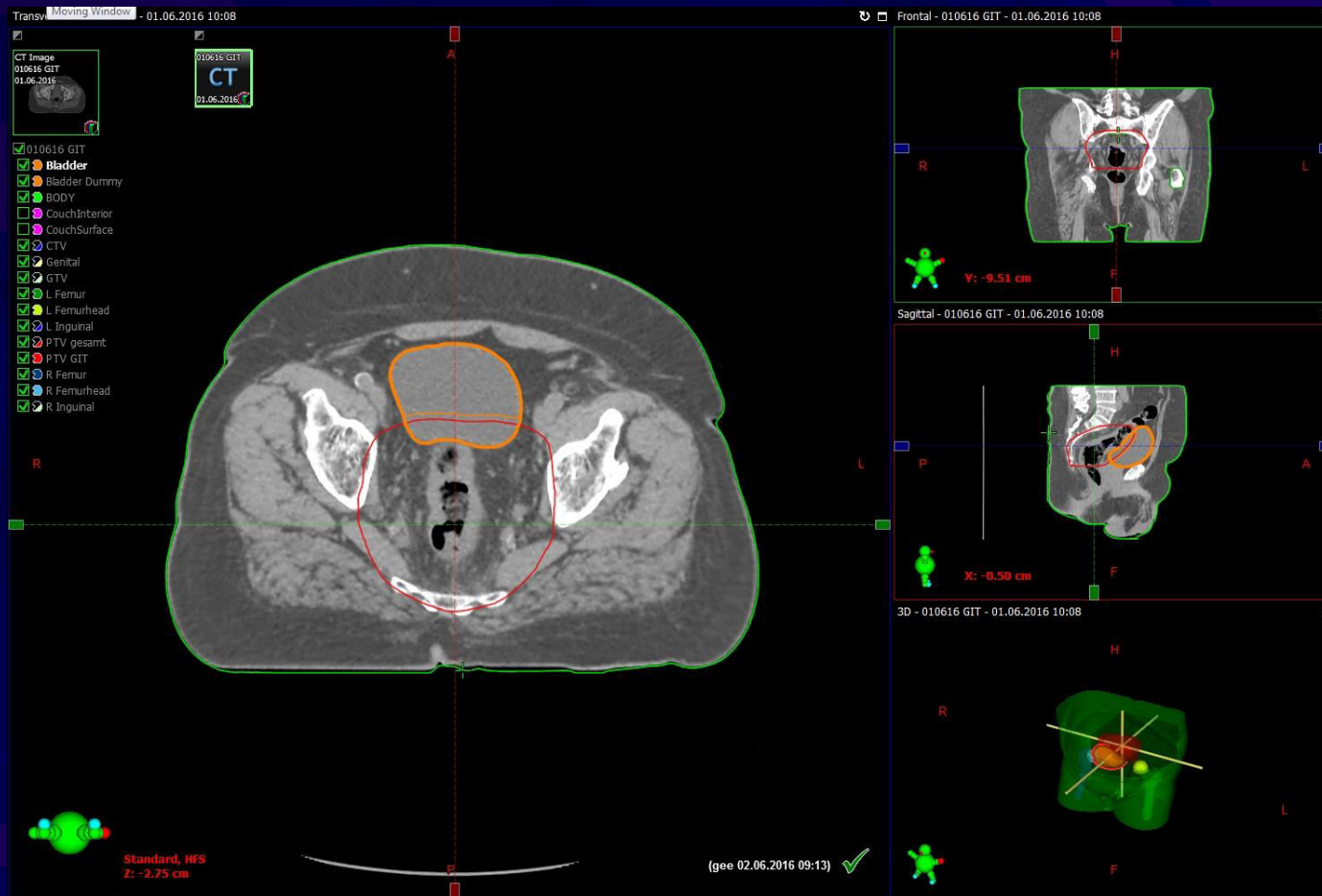
Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

Stadt+Wien
Wien ist anders.

Blasenschonung



Sphinkterschonung



Minimierung der Strahlenfolgen

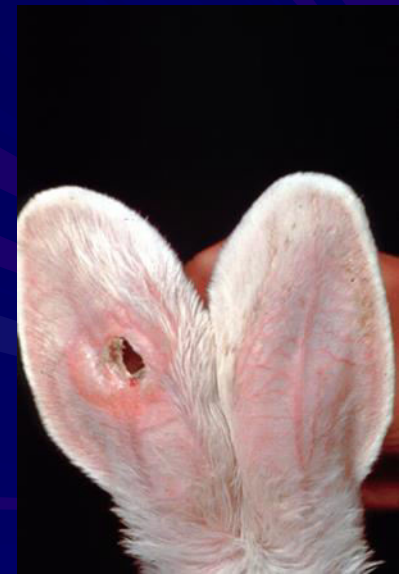
Adaptiertes Pflegekonzept befolgen

Lokalmaßnahmen-Vermeidung von

Chemische Reize: scharfes Essen, Fototoxische Substanzen
(z.B. Johanniskraut, Medikamente)

Mechanische Reize: Ballaststoffarme Ernährung, Enge Kleidung

Thermische Reize: Wärme ableiten (kalter Eichenrindentee)



Optimales Intervall zw RT und OP

- Metaanalyse Verlängerung des Intervalls auf > 8 Wochen erhöht

Petrelli F. et al, Metaanalyse Ann Surg 2016

- Höchster Tumorrespons: 7. – 10. Woche

Kwak YK, Kim K, Lee JH et al. Radiother Oncol. 2016

- 10-11 Wochen : höchste Rate an pCR

Sloothaak, Br J Surg 2013, 100: 933-030

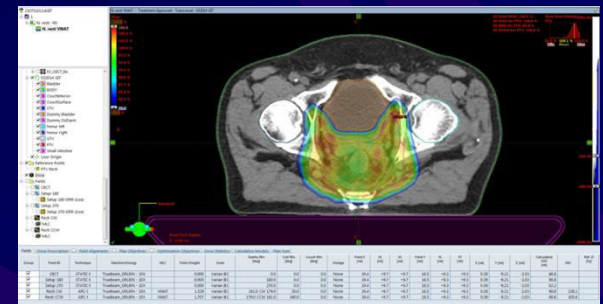
ASCO-A.De Vries

A randomized trial comparing mesorectal excision with or without lateral lymph node dissection for clinical stage II, III lower rectal cancer: Primary endpoint analysis of Japan Clinical Oncology Group study JCOG0212.

Fujita S, et al. J Clin Oncol 34, #3508

Lokalrezidivrate 7.1% vs 12.6%

Keine Vorbestrahlung



	ME+LLND (95% CI)	ME (95% CI)	HR (95% CI)
5-year RFS	73.4% (68.5-77.7%)	73.3% (68.3-77.6%)	1.07 (0.81-1.41)
5-year OS	92.6% (89.3-94.9%)	90.2% (86.5-92.9%)	1.25 (0.85-1.84)
5-year LRFS	87.7% (83.8-90.7%)	82.4% (78.0-86.1%)	1.37 (0.98-1.93)

Frage: Bestrahlungsvolumen Mesorektum plus Lymphknoten, braucht man dann eine lat Lymphadenektomie

ASCO-A.De Vries

- Immer mehr machen: Vorbestrahlung, wenn ypCR dann engmaschige Nachsorge, wenn Rezidiv Operation
- Anderer Denkansatz: kleine Tumore cT2 vorbestrahlen und dann nur noch lokal resezieren!

Wait and Watch od. trans-anale Excision

- Ältere Patienten
- Patienten mit Komorbiditäten
- Enges Follow up
- Salvage Operation(25%LR)
- Intensive Aufklärung!

Beets et al. when not to operate in rectal cancer, ESMO 2015
Angelita Habr Gama et al, Update 2014

Protonen?

J Gastrointest Oncol. 2014 Feb; 5(1): 3–8.

Protons offer reduced bone marrow, small bowel, and urinary bladder exposure for patients receiving neoadjuvant radiotherapy for resectable rectal cancer
Rovel J. Colaco, et al

Abstract

Background

To assess the potential benefit of proton therapy (PT) over photon therapy, we compared 3-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), and PT plans in patients undergoing neoadjuvant chemoradiation for resectable rectal cancer at our institution.

Methods

Eight consecutive patients with resectable (T2-T3) rectal cancers underwent 3DCRT, IMRT, and 3-dimensional conformal PT treatment planning. Initial target volumes (PTV1) were contoured using the Radiation Therapy Oncology Group anorectal atlas guidelines. Boost target volumes (PTV2) consisted of the gross rectal tumor plus a uniform 2-cm expansion. Plans delivered 45 Gray (Gy) or Cobalt Gray Equivalent (CGE) to the PTV1 and a 5.4-Gy (CGE) boost to the PTV2. Ninety-five percent of the PTVs received 100% of the target dose and 100% of the PTVs received 95% of the target dose. Standard normal-tissue constraints were utilized. Wilcoxon paired t-tests were performed to compare various dosimetric points between the 3 plans for each patient.

Results

All plans met all normal-tissue constraints and were isoeffective in terms of PTV coverage. The proton plans offered significantly reduced median normal-tissue exposure over the 3DCRT and IMRT plans with respect to pelvic bone marrow at the V5Gy, V10Gy, V15Gy, and V20Gy levels and the small bowel space at the V10Gy and V20Gy levels. The proton plans also offered significantly reduced median normal-tissue exposure over the 3DCRT plans with respect to the small bowel at the V30Gy and V40Gy levels and the urinary bladder at the V40Gy level.

Conclusions

By reducing bone marrow exposure, PT may reduce the acute hematologic toxicity of neoadjuvant chemoradiation and increase the likelihood of uninterrupted chemotherapy delivery. Bone marrow sparing may also facilitate the delivery of salvage chemotherapy for patients who subsequently develop hematogenous metastasis. Reduced small bowel exposure using PT may also reduce toxicity and possibly facilitate the use of more-aggressive chemotherapy with radiotherapy.

Nur Bestrahlungsplanvergleich-keine klinische Anwendung!!!

Neoadjuvante Radiotherapie – Vollremission bis Langzeitschaden

Zusammenfassung

- Warum präoperativ-dzt T3/T4/N+ Goldstandard
- Langzeit oder Kurzzeitvorbestrahlung-TU/Pat. Parameter
- Minimierung der Spätfolgen-multifaktorieller Einsatz
- Optimales Intervall zw RT und OP-warten-warten!min.8 Wo
- ASCO 2016 ev.Bestrahlung lat. LYKNO
- Wait and Watch od. trans-anale Excision-Erfahrungen
- Protonen-Keine Indikation

THE HUMAN FACTOR.....



THE HUMAN FACTOR.....



ypT1, ypT2 (i.e., G1-2, vs G3, absence vs presence of lymphovascular invasion) has been reported[140]. The presence of lymphovascular invasion, as well as a poor tumour differentiation are well-known prognostic factors for risk of nodal metastases after neoadjuvant chemotherapy followed by TME and local excision and should be taken into account when considering a trans-anal excision

World J Gastroenterol. 2014 Aug 28; 20(32): 11249–11261.

Multidisciplinary treatment of rectal cancer in 2014: Where are we going?

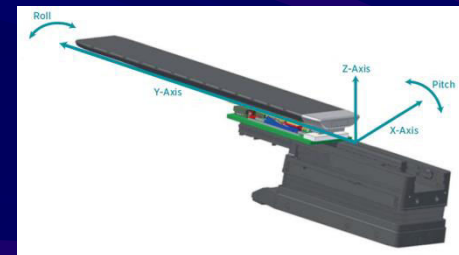
Andrea Vignali and Paola De Nardi

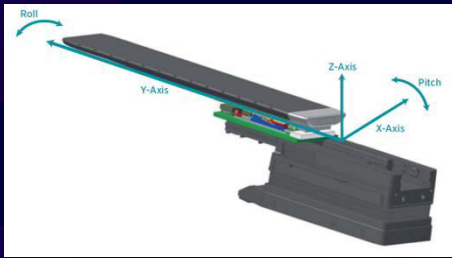
Stereotaxie ist gemäß der DEGRO-Leitlinien von 2014 eine kleinvolumige Bestrahlung im Sinne einer Hochpräzisionsstrahlentherapie mit minimalen Sicherheitsabständen, hohen Bestrahlungsdosen am Tumor und wenigen Bestrahlungsfractionen (2-max.3x/Woche)

CBCT Verschiebungen

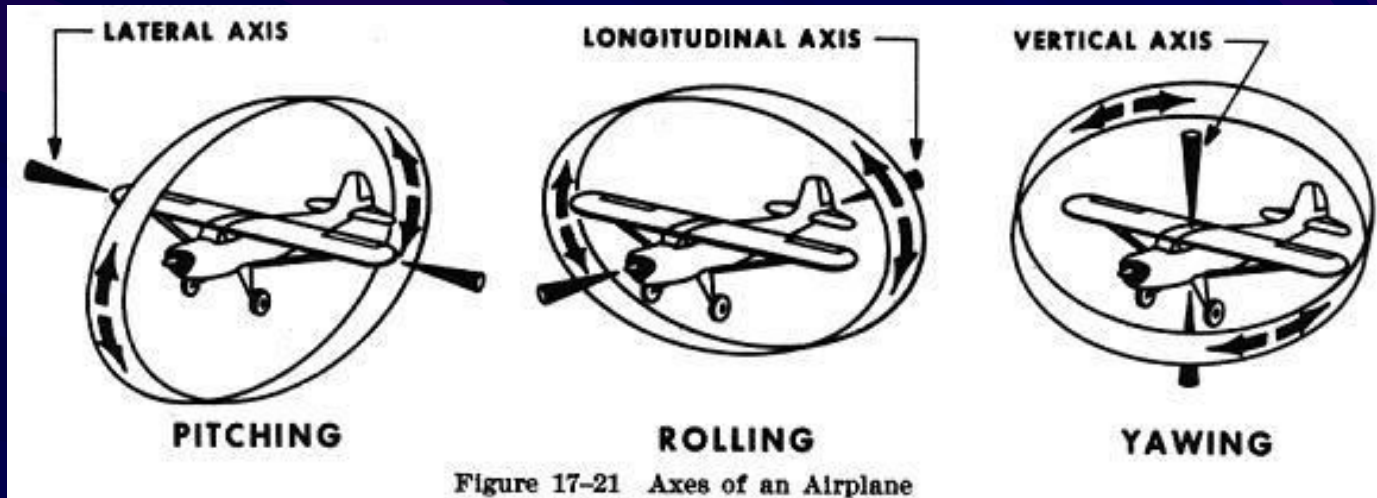
- Tägliche 6D Korrekturen mittels CBCT bei Patienten mit primärem Prostatakarzinom (C61) und Rektumkarzinom (C20)

Varian 6D Couch





Achsrotationen



- Pitch ...Rotation um die laterale Achse(X)
- Roll ...Rotation um die longitudinale Achse(Y)
- Yaw ...Rotation um die vertikale Achse(Z) (im Folgenden „Rotation“ oder „Rtn“)

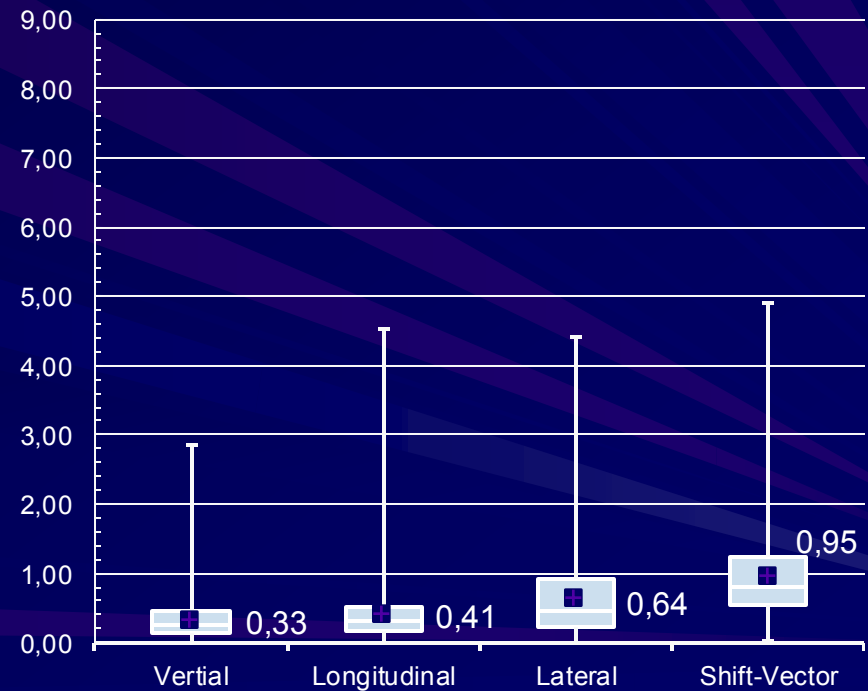
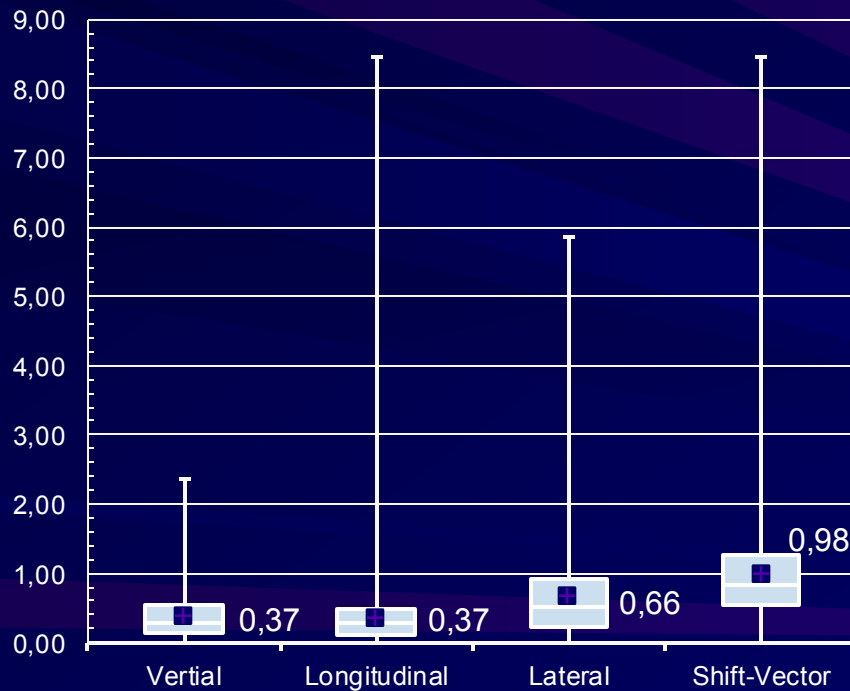
Vergleich Translationen

■ Prostata (n=1470)

■ Recti (n=761)

Translationen [cm]

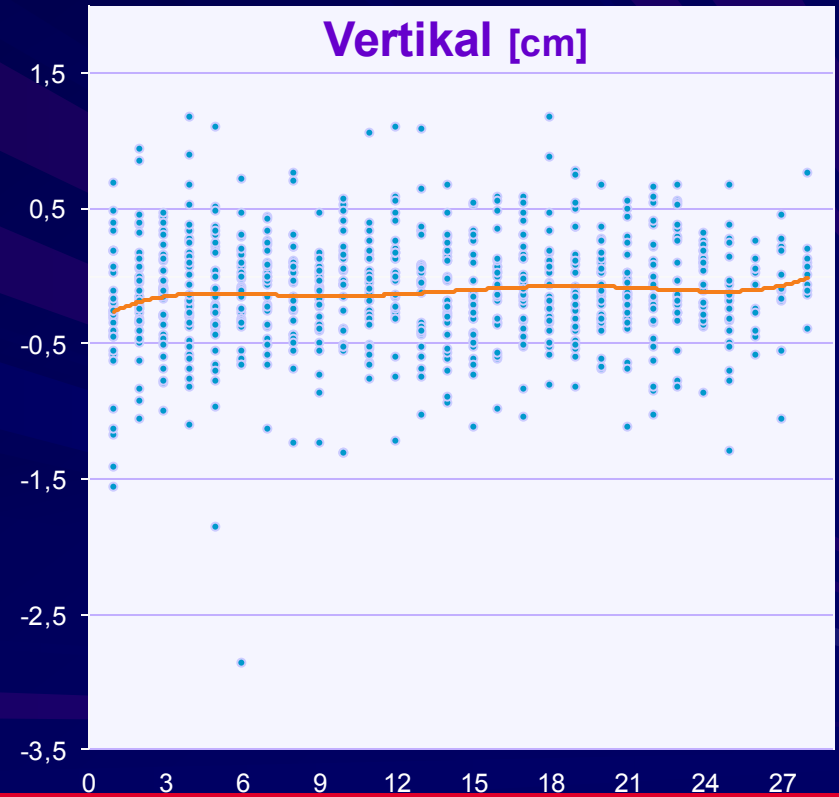
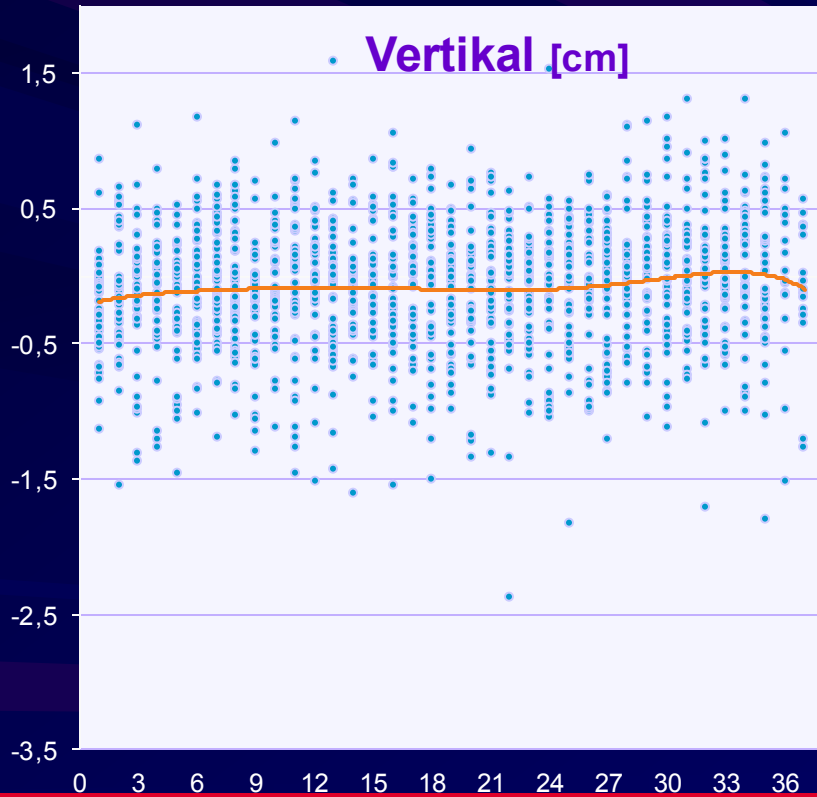
Translationen [cm]



Fraktionsabhängigkeit

■ Prostata (n=1470)

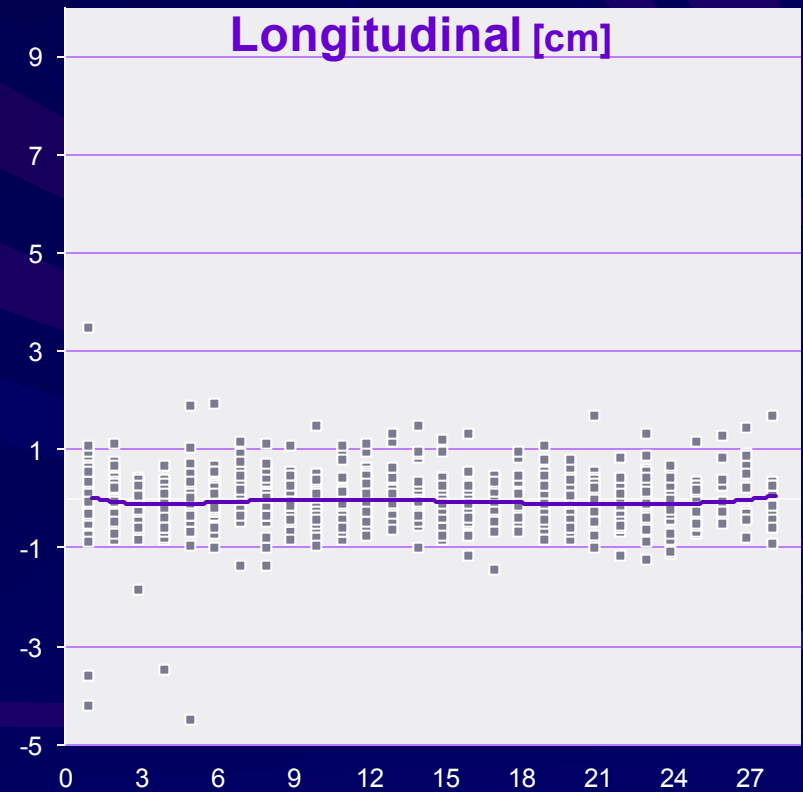
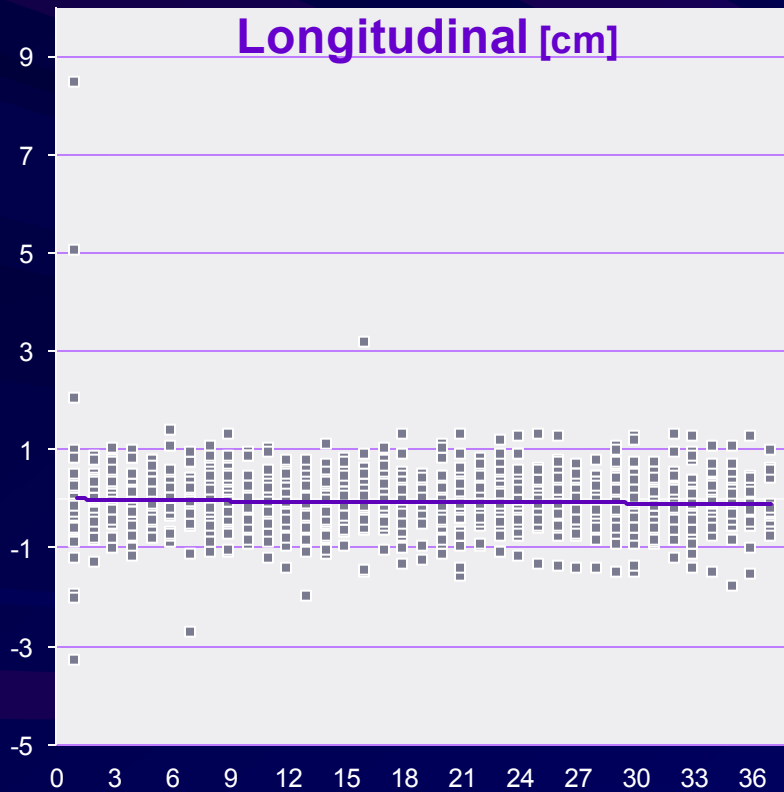
■ Recti (n=761)



Fraktionsabhängigkeit

■ Prostata (n=1470)

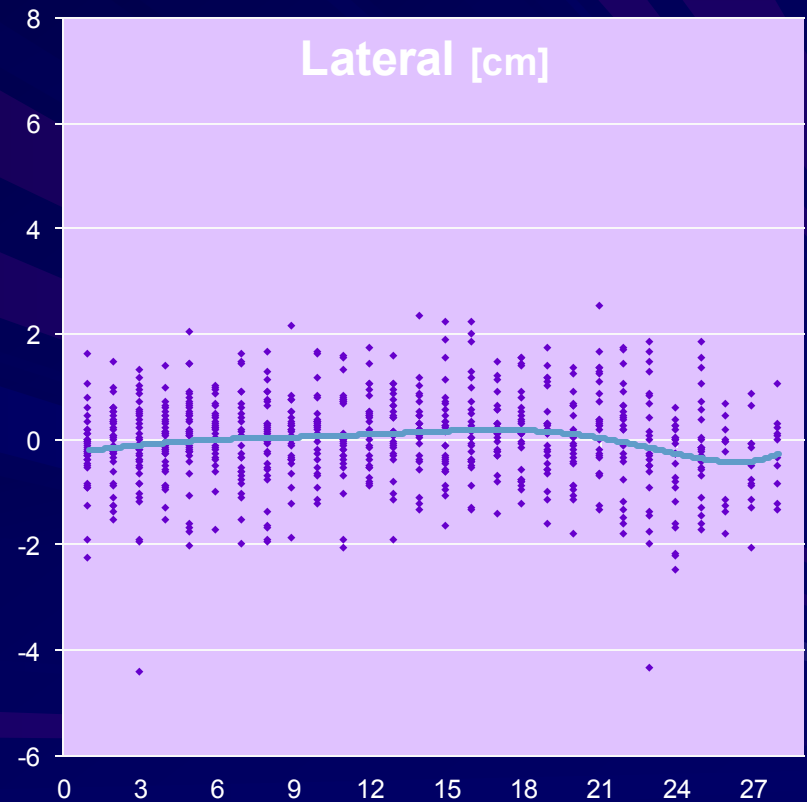
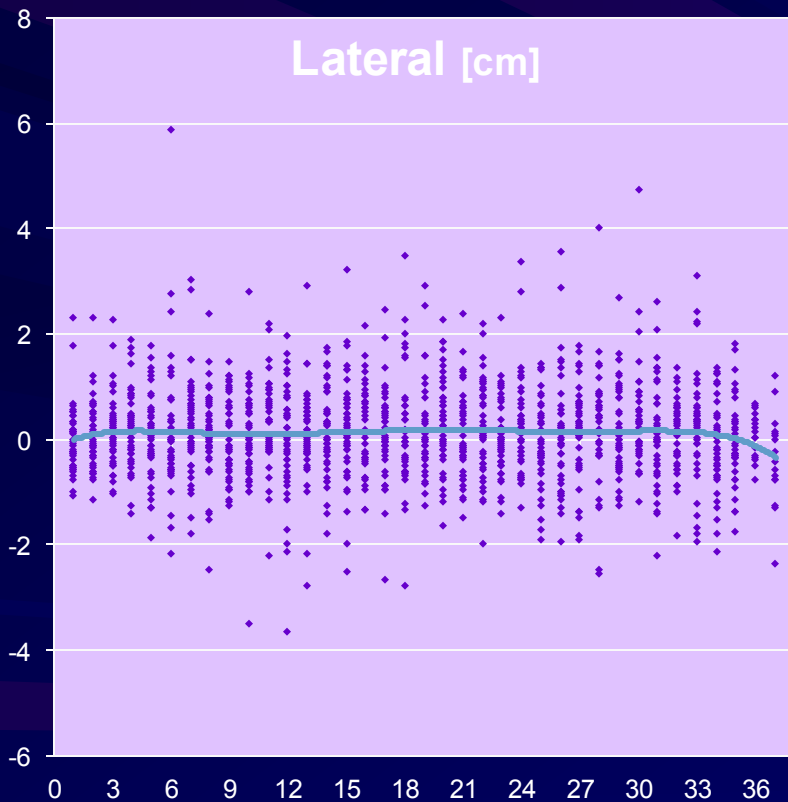
■ Recti (n=761)



Fraktionsabhängigkeit

■ Prostata (n=1470)

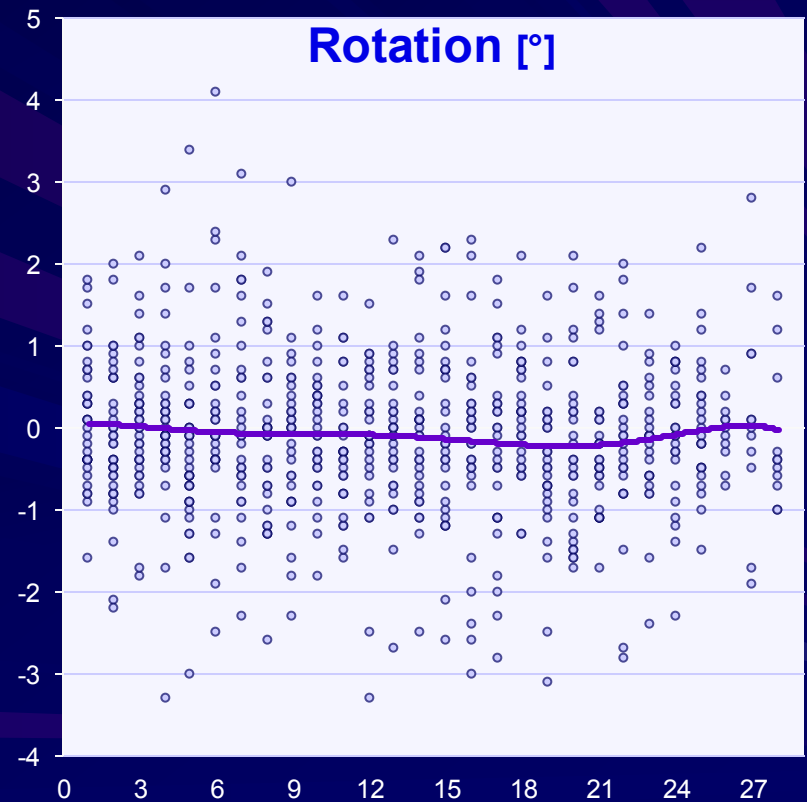
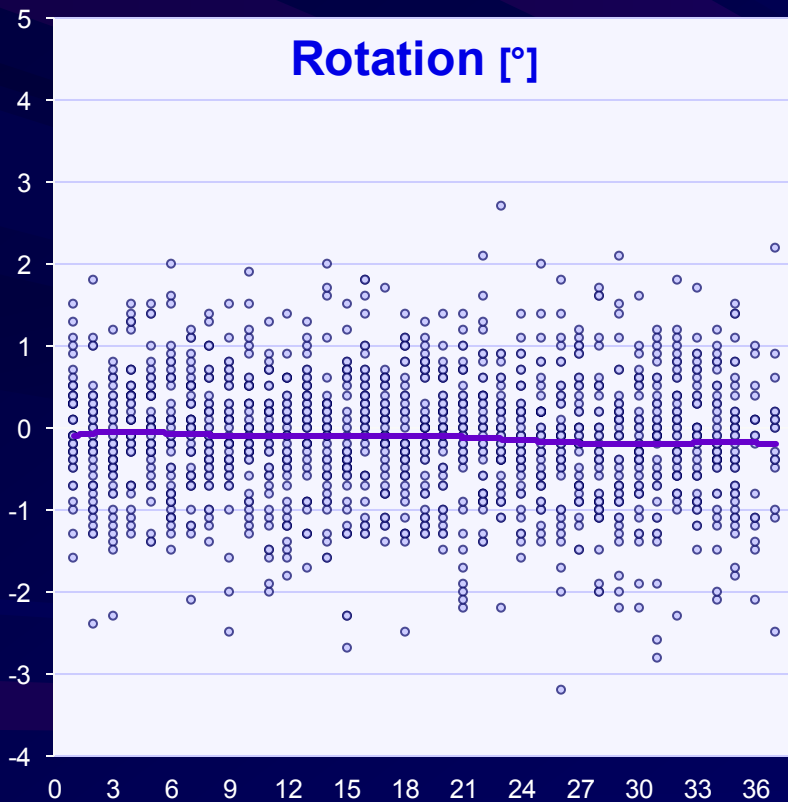
■ Recti (n=761)



Fraktionsabhängigkeit

■ Prostata (n=1470)

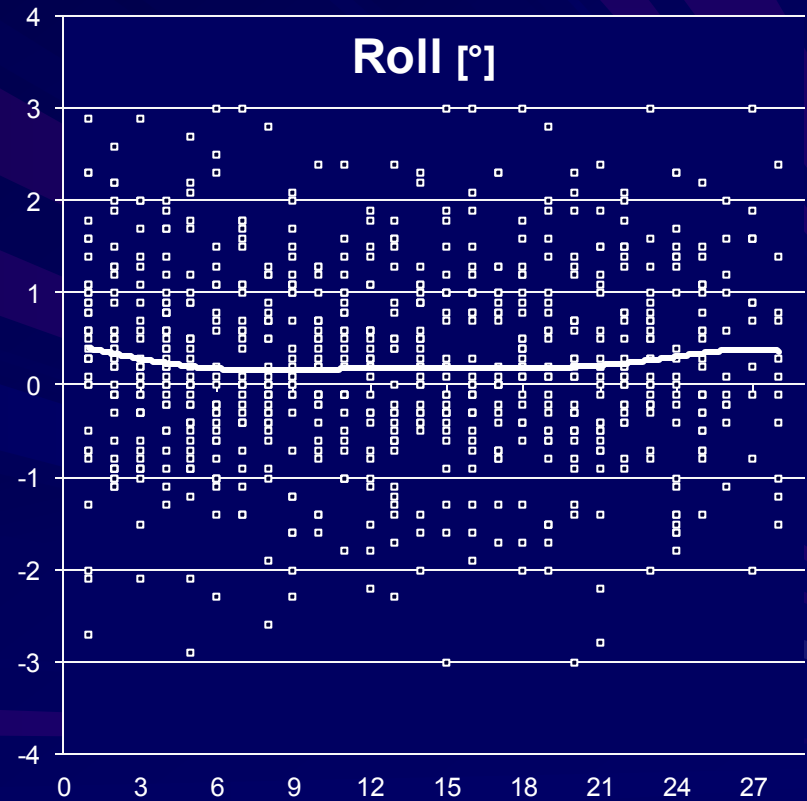
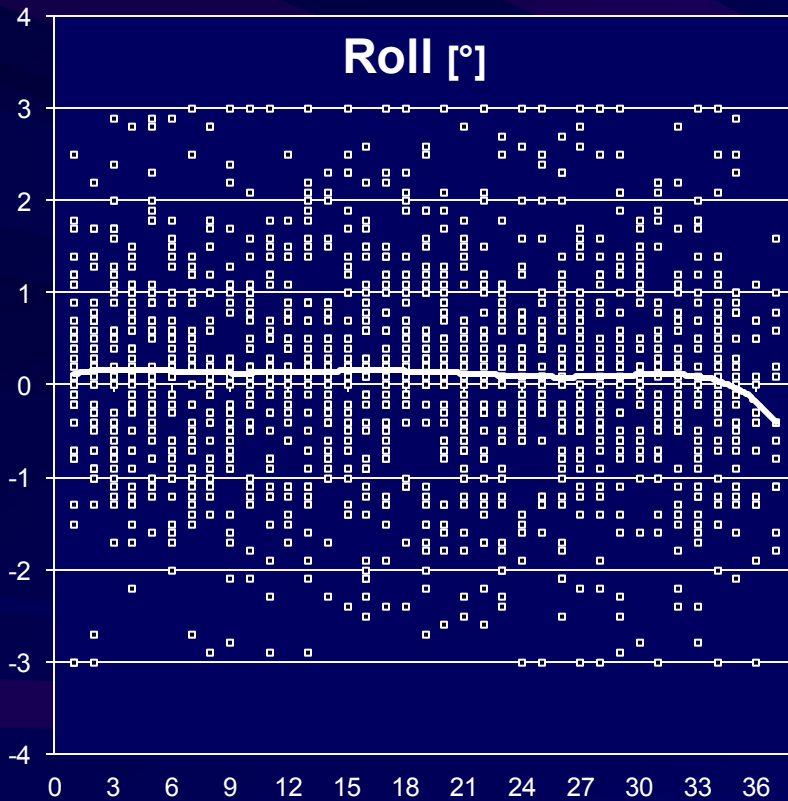
■ Recti (n=761)



Fraktionsabhängigkeit

■ Prostata (n=1470)

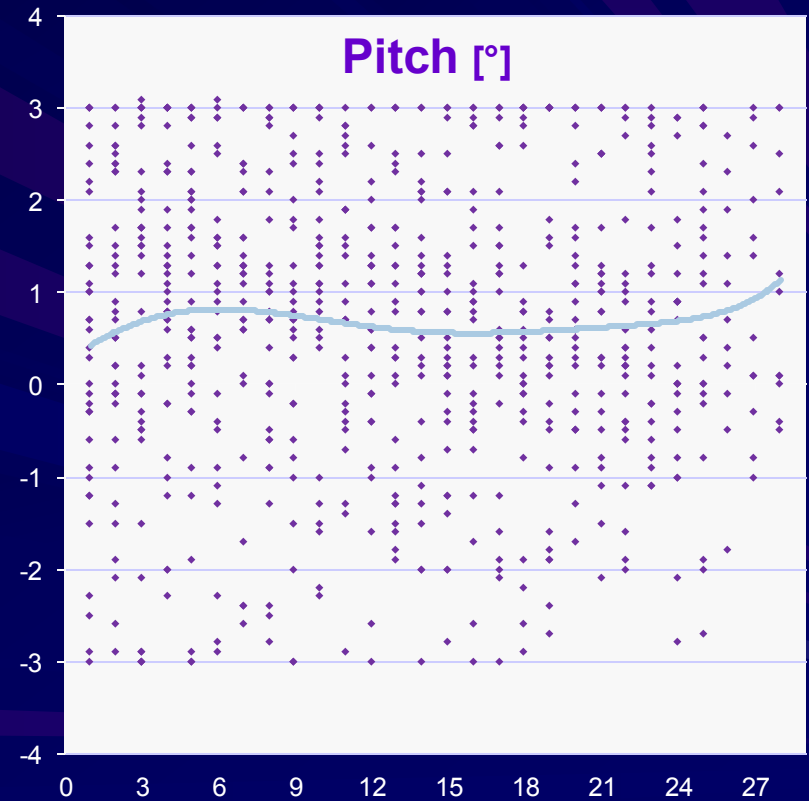
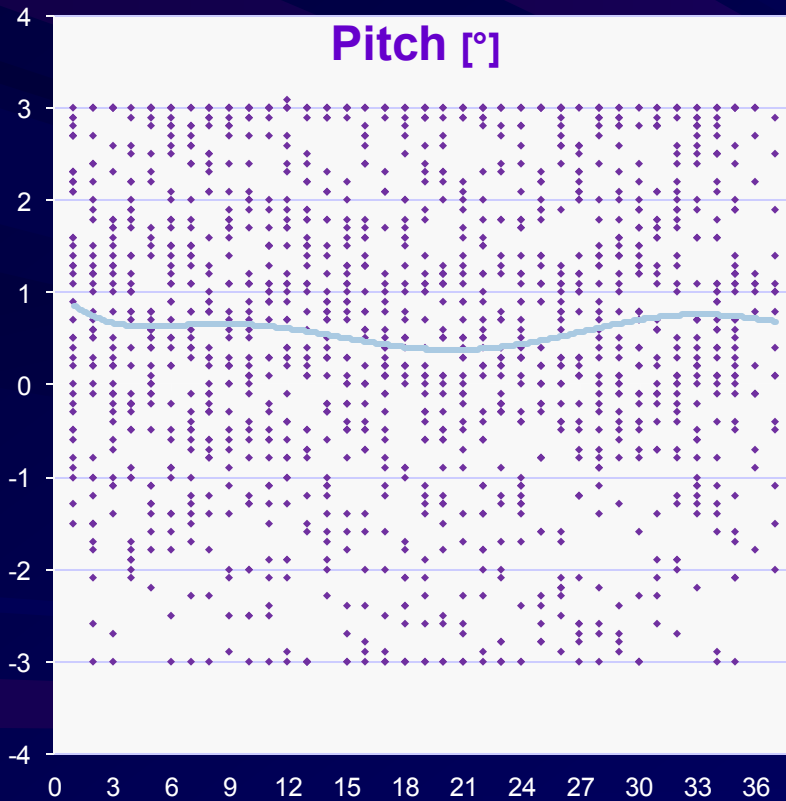
■ Recti (n=761)



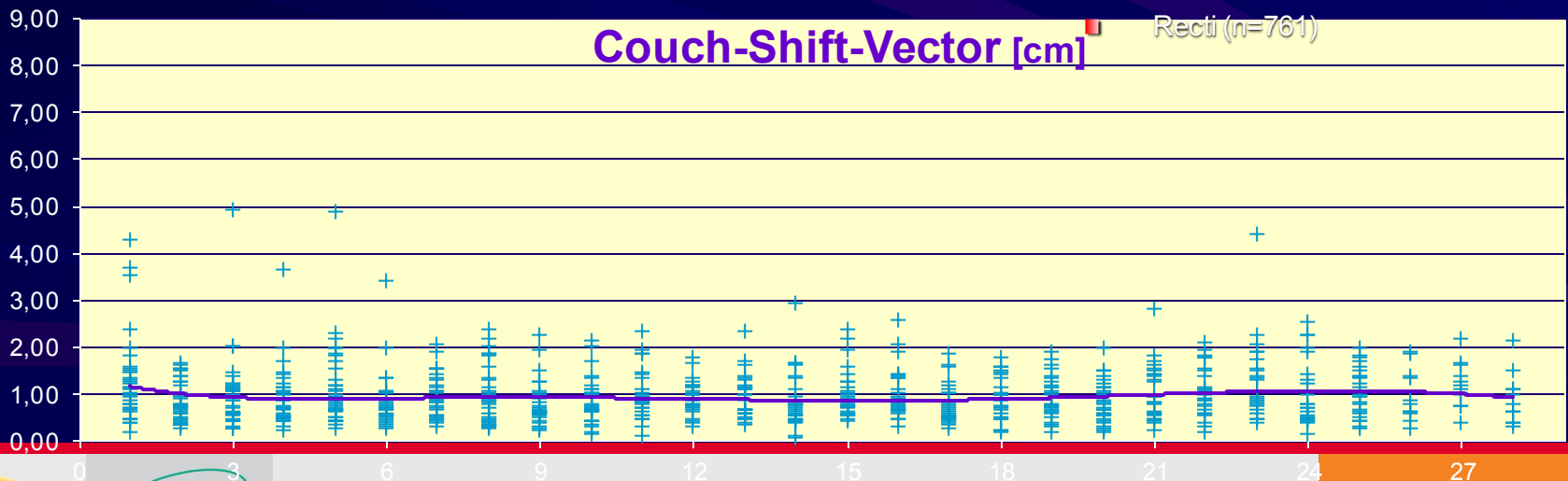
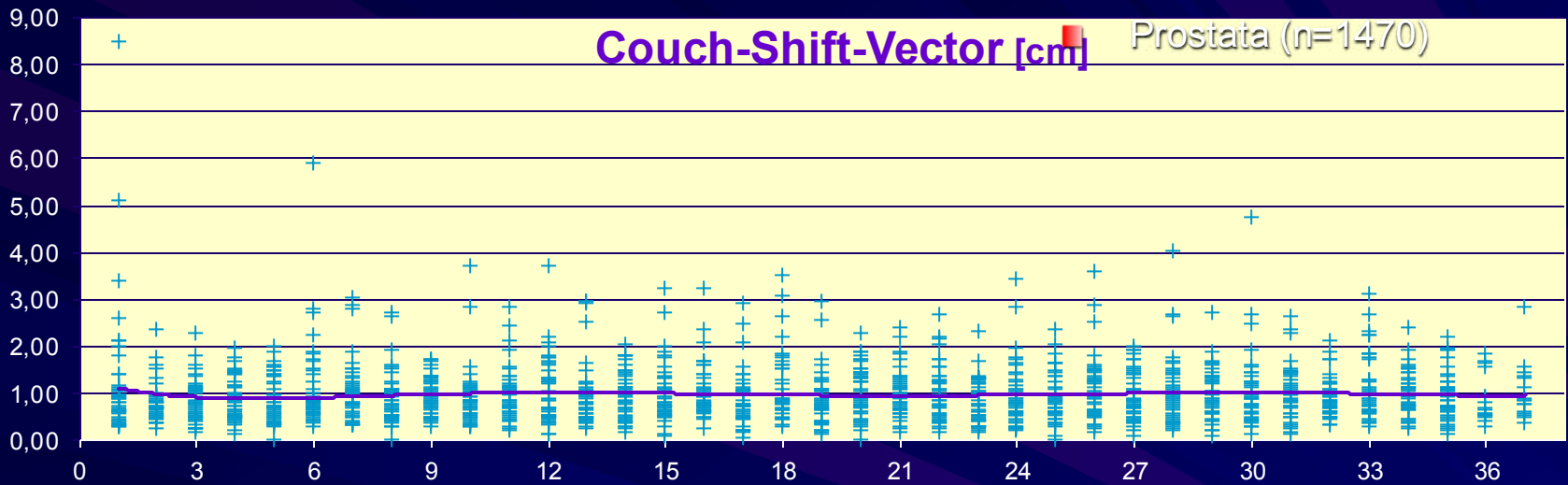
Fraktionsabhängigkeit

■ Prostata (n=1470)

■ Recti (n=761)

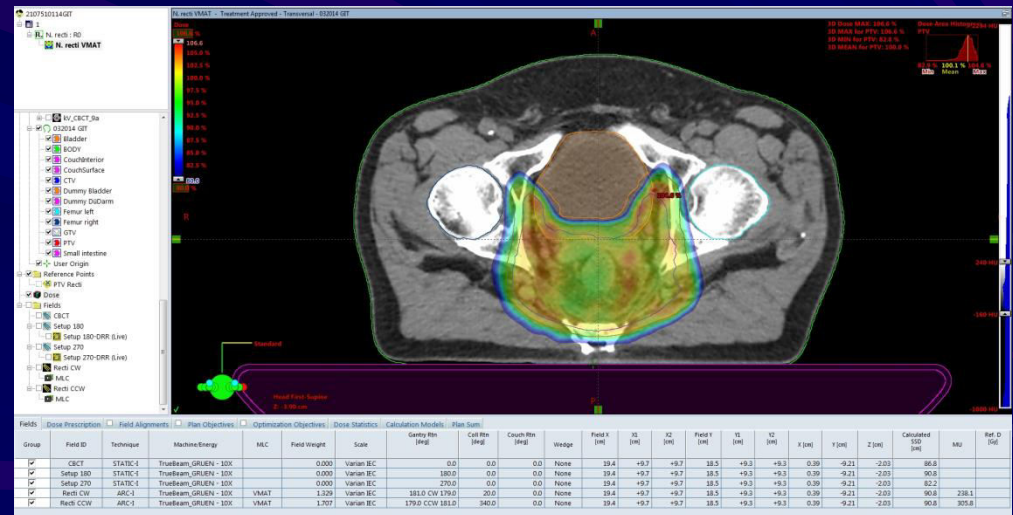


Fraktionsabhängigkeit

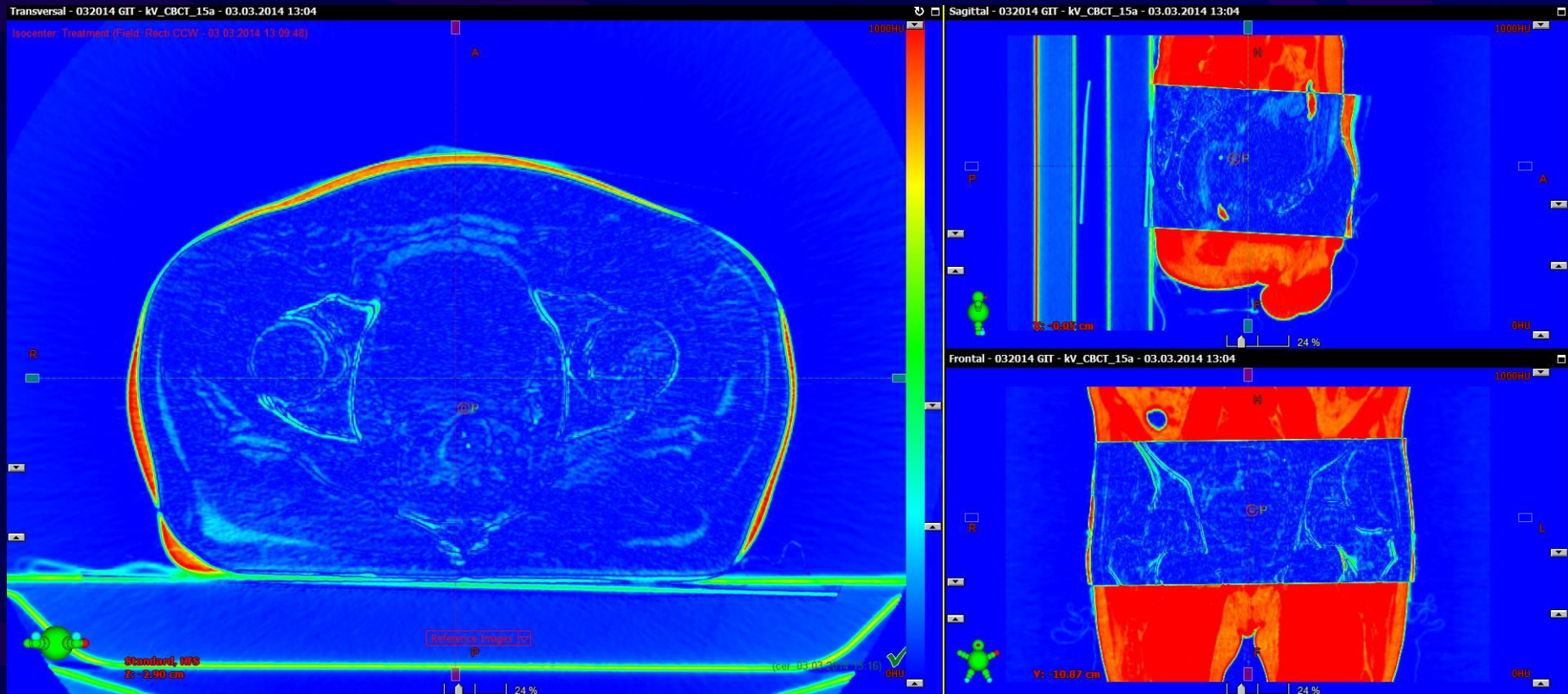


Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

80% Isodose Rektum



Bilddifferenz

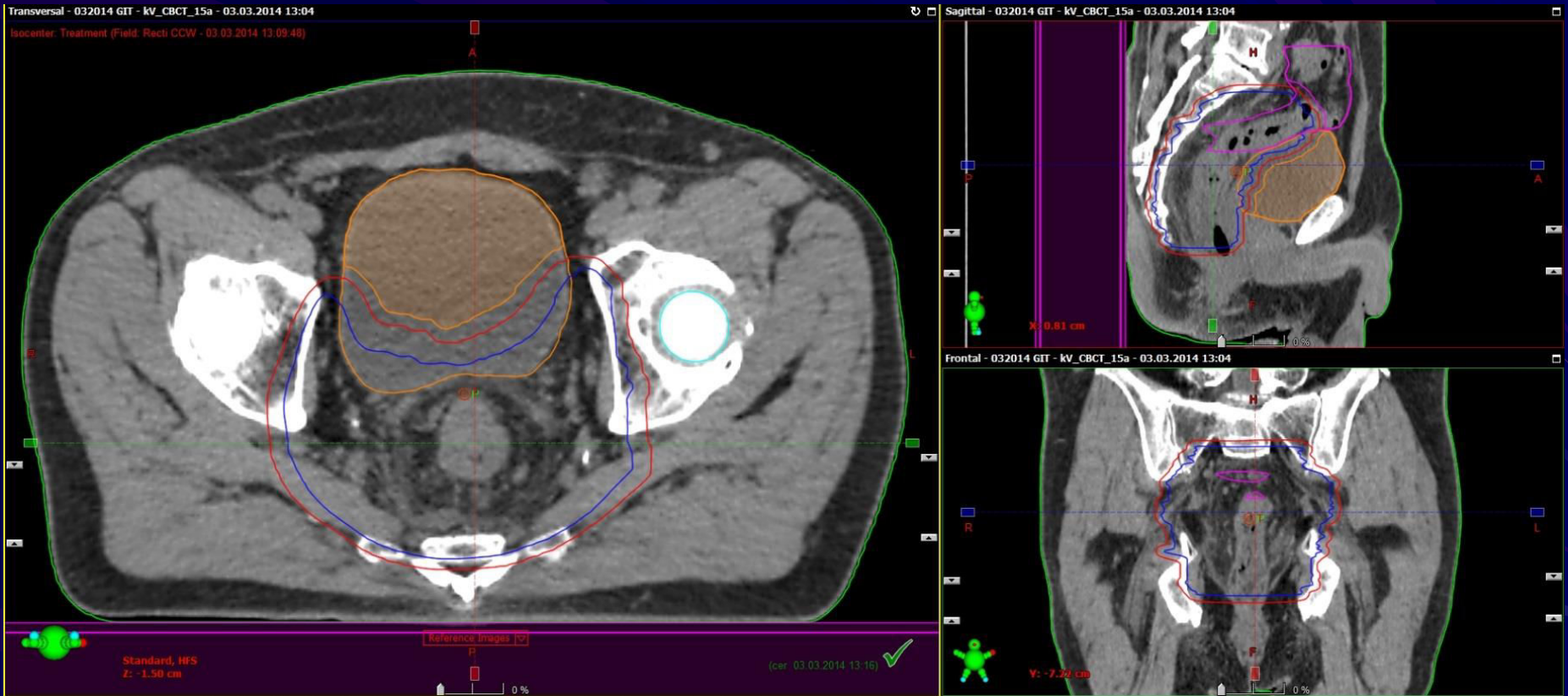


Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

Stadt+Wien
Wien ist anders.



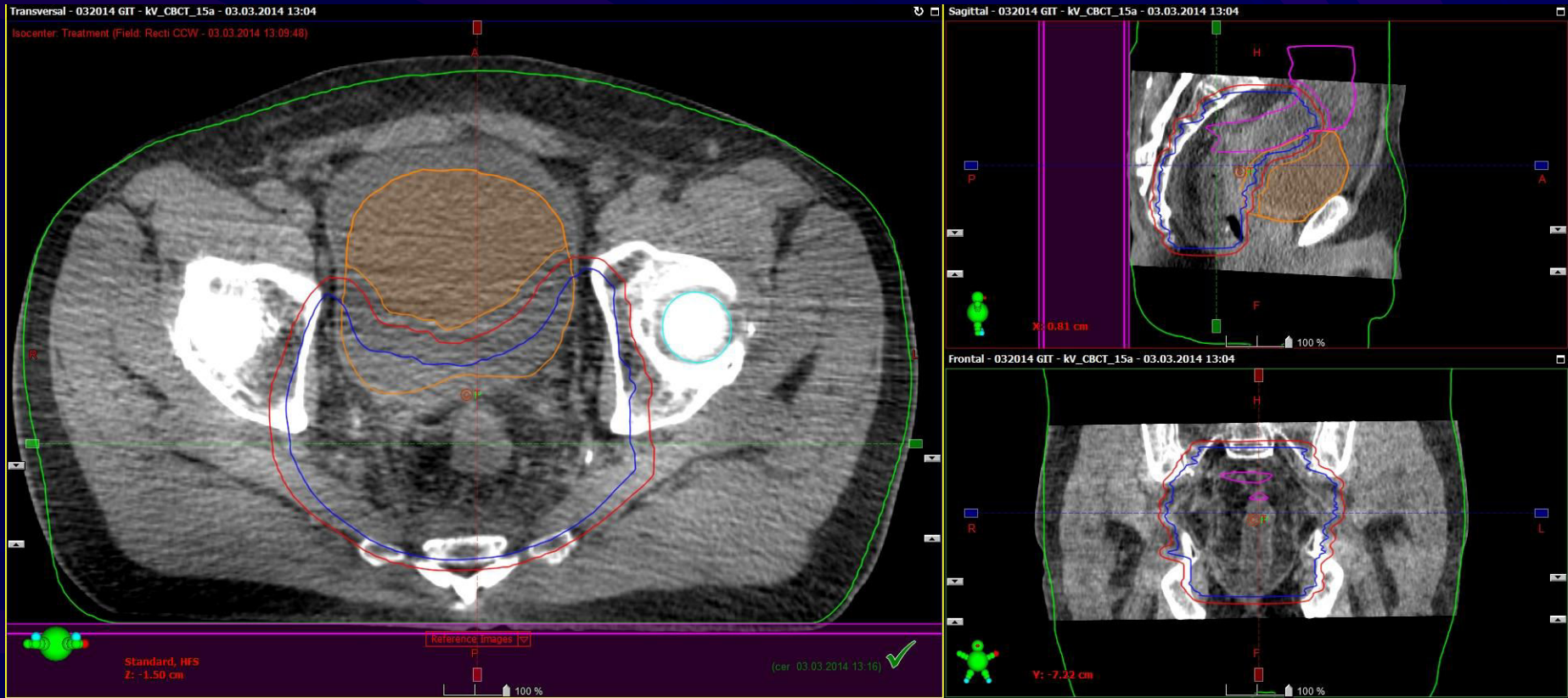
Referenzbild



Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

Stadt+Wien
Wien ist anders.

CTBC



Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

Stadt+Wien
Wien ist anders.

Minimierung der Strahlenfolgen

Rektum: Tenesmen, Multistuhlfrequenz, Schleimhautblutungen

Dünndarm: Fibrosierungen, Stenosierungen, Fistelbildungen, Ileus

Sphinkter: Fibrosierungen, Stenosen, Sphinkterschwäche (2% nach coloanal Anastomosen)

Blase: Schrumpfbhase, Schleimhautblutungen

Sexualfunktion: Spätfolgen nach mehreren Jahren (erektiler Dysfunktion)

Akutreaktionen

Rektum: 5% Wundheilungsstörungen im Anastomosensbereich (passagere Colostomie), kein Neorektumpouch (Stuhlkapazitätnormalisierung nach 6 Monaten)

Blase: Zystitische Beschwerden

Dünndarm: Diarrhoen

Can chemoradiation allow for omission of lateral pelvic node dissection for locally advanced rectal cancer?

Abstract

OBJECTIVES:

We evaluated the relationship between pretreatment clinical parameters and lateral pelvic node (LPN) recurrence in patients with rectal cancer treated with a combination of curative resection and chemoradiotherapy (CRT) and attempted to identify the patients who might benefit from LPN dissection.

METHODS:

This study involved 900 patients between June 2001 and June 2009. Pretreatment clinical parameters including radiological size of LPN were analyzed to identify risk factors associated with long-term outcomes.

RESULTS:

Locoregional recurrence developed in 65 patients (7.2%); 42 (64.6%) had LPN recurrence, 20 (47.6%) of which had no distant metastasis. Multivariate analysis showed that LPN short-axis diameter (<5, 5-<10, and ≥ 10 mm) was significantly associated with LPN recurrence-free survival (5-year survival rate (5YSR), 98.2, 91.7, and 40.1%, respectively, $P < 0.05$), locoregional recurrence-free survival (5YSR, 95.5, 87.6, and 40.1%, respectively, $P < 0.05$), relapse-free survival (5YSR, 76.8, 72.5, and 30.3, respectively, $P < 0.05$), and overall survival (5YSR, 86.3, 83.0, and 57.5%, respectively, $P < 0.05$).

CONCLUSIONS:

Patients with an LPN short-axis diameter ≥ 10 mm represent a potential subgroup at a high risk of LPN recurrence, even after CRT. Further study is needed to confirm whether LPN dissection is beneficial for these patients.

J Surg Oncol. 2015 Mar 15;111(4):459-64. doi: 10.1002/jso.23852. Epub 2015 Jan 5; Kim MJ et al.

Neoadjuvant chemoradiotherapy affects the indications for lateral pelvic node dissection in mid/low rectal cancer with clinically suspected lateral node involvement: a multicenter retrospective cohort study

Abstract

BACKGROUND:

Although lateral pelvic node dissection (LPND) is recommended for rectal cancer with clinically metastatic lateral pelvic lymph nodes (LPNs), LPNs may respond to neoadjuvant chemoradiotherapy (nCRT). Our aim was to determine the optimal indication for LPND after nCRT for mid/low rectal cancer.

METHODS:

Of 2,263 patients with clinical stage II/III mid/low rectal cancer who were managed at three tertiary referral hospitals, 66 patients underwent curative surgery including LPND after nCRT were included in this study. Risk factors for LPN metastasis were retrospectively analyzed and oncologic outcomes determined according to LPN response to nCRT.

RESULTS:

Persistent LPNs greater than 5 mm on post-nCRT magnetic resonance imaging were significantly associated with residual tumor metastasis, unlike responsive LPN after nCRT (short-axis diameter ≤ 5 mm) (pathologically, 61.1 % [22 of 36] vs. 0 % [0 of 30], $P < 0.001$). Multivariable analysis revealed post-nCRT LPN size as a significant and independent risk factor for LPN metastasis (odds ratio 2.390; 95 % confidence interval 1.104-4.069). Over a median follow-up of 39.3 months, the recurrence rate was lower in patients with responsive nodes than in patients with persistent nodes (20 % [6 of 30] vs. 47.2 % [17 of 36], $P = 0.012$). The 5-year overall survival and 5-year disease-free survival rates were lower in patients with persistent LPN than in patients with responsive LPN (44.6 % vs. 77.1 %, $P = 0.034$; 33.7 % vs. 72.5 %, $P = 0.011$, respectively).

CONCLUSIONS:

In mid/low rectal cancer with clinically metastatic LPNs, the decision to perform LPND should be based on the LPN response to nCRT.

Ann Surg Oncol. 2014 Jul;21(7):2280-7. doi: 10.1245/s10434-014-3559-z. Epub 2014 Mar 7; Oh HK et al.

Treatment Interval between Neoadjuvant Chemoradiotherapy and Surgery in Rectal Cancer Patients: A Population-Based Study

Abstract

BACKGROUND:

Neoadjuvant chemoradiation therapy (CRT) has been widely implemented in the treatment of rectal cancer patients, but optimal timing of surgery after neoadjuvant therapy is unclear. The purpose of this study was to evaluate the effects of prolonged intervals between long-course CRT and surgery in rectal cancer patients.

METHODS:

Data on all rectal cancer patients diagnosed between 2006 and 2011 were retrieved from the population-based Netherlands Cancer Registry; the main outcome parameters were pathologic complete response (pCR) and overall survival (OS). Outcomes were reported separately for patients with early tumors (ETs; N = 217) and locally advanced rectal cancer (LARC; N = 1073). Patients were divided into 2-week interval groups according to treatment interval, ranging from 5-6 to 13-14 weeks. Kaplan-Meier curves, and logistic regression and Cox regression models were used for data analysis.

RESULTS:

No significant difference in pCR rate was observed for ET patients according to treatment interval. Compared with a treatment interval of 7-8 weeks, pCR rates in LARC patients were higher after 9-10 weeks (18.4 %; odds ratio [OR] 1.56, 95 % CI 1.03-2.37) and 11-12 weeks of treatment interval (20.8 %; OR 1.94, 95 % CI 1.15-3.26). Treatment interval did not influence OS in ET or LARC patients.

CONCLUSIONS:

Treatment intervals of 9-12 weeks between surgery and CRT seem to improve the chances of pCR in LARC patients, without an effect on OS. The length of treatment interval did not affect outcomes in patients with ET. The ongoing search for minimally invasive surgery drives the need for exploration of factors that improve pathologic response.

[See comment in PubMed Commons below Ann Surg Oncol. 2016 Jun 1. \[Epub ahead of print\]; Rombouts AJ et al.](#)

Increasing the Interval Between Neoadjuvant Chemoradiotherapy and Surgery in Rectal Cancer: A Meta-analysis of Published Studies

Abstract

OBJECTIVE:

The aim of this meta-analysis was to demonstrate whether a longer interval between the end of neoadjuvant chemoradiotherapy (CRT) and surgery is associated with a better rate of pathological complete response (pCR) in rectal cancer.

BACKGROUND:

The standard of care in locally advanced rectal cancer is preoperative, long course (5-fluorouracil-based) CRT. After this neoadjuvant CRT, surgical exploration is undertaken 6 to 8 weeks later.

METHODS:

PubMed, EMBASE, the ISI Web of Science, and The Cochrane Library (CENTRAL) were searched systematically for prospective or retrospective studies reporting oncological results for intervals longer or shorter than 6 to 8 weeks between the end of CRT and surgery, in rectal cancer. The primary endpoint, reported as relative risk (RR), was the rate of pCR. Secondary endpoints were overall survival (OS), disease-free survival (DFS), R0 resection rates, sphincter preservations, and wound/anastomotic complications. A meta-analysis was performed, using the fixed- or random-effects model, with Review Manager 5.1.

RESULTS:

Thirteen trials, including 3584 patients, were identified, and overall, an interval longer than 6 to 8 weeks from the end of neoadjuvant CRT and surgery significantly improved the pCR (RR = 1.42, 95% confidence interval: 1.19-1.68; $P < 0.0001$). Pathological complete responses increased from 13.7% to 19.5% in the longer interval group, and the OS, DFS, R0 resection rates, sphincter preservation, and complication rates were similar in the 2 groups.

CONCLUSIONS:

A longer waiting interval (more than the classical 6-8 weeks) from the end of preoperative CRT increases the rate of pCR by 6% in rectal cancer, with similar outcomes and complication rates. These results should be validated prospectively in a randomized trial.

Ann Surg. 2016 Mar;263(3):458-64. doi: 10.1097/SLA.0000000000000368; Petrelli F et al.

Effect of Interval between Neoadjuvant Chemoradiotherapy and Surgery on Oncological Outcome for Rectal Cancer: A Systematic Review and Meta-Analysis

Abstract

Aim. To evaluate the influence of interval between neoadjuvant chemoradiotherapy (NCRT) and surgery on oncological outcome. **Methods.** A systematic search was conducted in PubMed, the Cochrane Library, and Embase databases for publications reporting oncological outcomes of patients following rectal cancer surgery performed at different NCRT-surgery intervals. Relative risk (RR) of pathological complete response (pCR) among different intervals was pooled. **Results.** Fifteen retrospective cohort studies representing 4431 patients met the inclusion criteria. There was a significantly increased rate of pCR in patients treated with surgery followed 7 or 8 weeks later (RR, 1.45; 95% CI, 1.18-1.78; and $P < 0.01$ and RR, 1.49; 95% CI, 1.15-1.92; and $P = 0.002$, resp.). There is no consistent evidence of improved local control or overall survival with longer or shorter intervals. **Conclusion.** Performing surgery 7-8 weeks after the end of NCRT results in the highest chance of achieving pCR. For candidates of abdominoperineal resection before NCRT, these data support implementation of prolonging the interval after NCRT to optimize the chances of pCR and perhaps add to the possibility of ultimate organ preservation.

[Gastroenterol Res Pract.](#) 2016;2016:6756859. doi: 10.1155/2016/6756859. Epub 2016 Mar 30; Wang XJ et al.

Changes in treatment patterns for patients with locally advanced rectal cancer in the United States over the past decade: An analysis from the National Cancer Data Base

Abstract

BACKGROUND:

In the United States, neoadjuvant chemoradiotherapy (NACRT) is widely accepted as the standard of care in the treatment of patients with locally advanced rectal cancer. In the current study, the authors attempted to examine patterns of treatment in the United States over the past decade.

METHODS:

Using the National Cancer Data Base, a total of 66,197 patients who were diagnosed with American Joint Committee on Cancer stage II to III rectal adenocarcinoma and treated between 2004 and 2012 were identified. The authors described trends in the receipt of treatment for 3 time periods (2004-2006, 2007-2009, and 2010-2012) and analyzed 5-year overall survival probabilities for 28,550 patients treated between 2004 and 2007.

RESULTS:

Receipt of NACRT increased significantly from 42.9% between 2004 and 2006 to 50.0% between 2007 and 2009, and to 55.0% between 2010 and 2012 ($P < .0001$). In contrast, the use of adjuvant chemoradiotherapy (CRT) decreased from 16.7% between 2004 and 2006 to 10.5% between 2007 and 2009, and to 6.7% between 2010 and 2012 ($P < .0001$). Similarly, the use of surgery alone decreased from 13.1% between 2004 and 2006 to 8.7% between 2010 and 2012 ($P < .0001$). Older age, the presence of comorbidities, larger primary tumor size, lymph node involvement, not being of non-Hispanic white race/ethnicity, lack of private insurance, and treatment at a facility that did not have a high case volume were associated with a significantly lower possibility of receiving NACRT. The 5-year overall survival rates for patients treated with NACRT, surgery and adjuvant CRT, surgery alone, and definitive CRT were 72.4%, 70.9%, 44.9%, and 48.8%, respectively.

CONCLUSIONS:

The use of NACRT before surgery in US patients with rectal cancer has substantially increased over the past decade. However, only approximately one-half of patients currently receive this standard therapy, which could be explained in part by socioeconomic factors. Trimodality therapy is associated with the best outcomes for these patients. Cancer 2016. © 2016 American Cancer Society.

[See comment in PubMed Commons below Cancer](#). 2016 Apr 13. doi: 10.1002/cncr.29993. [Epub ahead of print]; Sineshaw HMet al.

The effects of neoadjuvant chemoradiotherapy on physical fitness and morbidity in rectal cancer surgery patients

Abstract

BACKGROUND:

Neoadjuvant chemoradiotherapy (NACRT) followed by surgery for resectable locally advanced rectal cancer improves outcome compared with surgery alone. Our primary hypothesis was that NACRT impairs objectively-measured physical fitness. We also wished to explore the relationship between fitness and postoperative outcome.

METHOD:

In an observational study, we prospectively studied 27 consecutive patients, of whom 25 undertook cardiopulmonary exercise testing (CPET) 2 weeks before and 7 weeks after standardized NACRT, then underwent surgery. In-hospital post-operative morbidity and mortality were recorded. Patients were followed up to 1 year for mortality. Data was analysed blind to clinical details. Receiver-operating characteristic (ROC) analysis defined the predictive value of CPET for in-hospital morbidity at day 5.

RESULTS:

Oxygen uptake ([Formula: see text] in ml kg⁻¹ min⁻¹) at estimated lactate threshold (θ^L) and at peak exercise ([Formula: see text] at peak in ml kg⁻¹ min⁻¹) both significantly decreased post-NACRT: [Formula: see text] at θ^L 12.1 (pre-NACRT) vs. 10.6 (post-NACRT), $p < 0.001$ (95%CI -1.7, -1.2); [Formula: see text] at peak 18.1 vs. 16.7, $p < 0.001$ (95%CI -3.1, -1.0). Optimal [Formula: see text] at θ^L and peak pre-NACRT for predicting postoperative morbidity were 12.0 and 18.1 ([Formula: see text] at θ^L - AUC = 0.71, 77% sensitive and 75% specific; [Formula: see text] at peak - AUC = 0.75, 78% sensitive and 76% specific). Optimal [Formula: see text] at θ^L and peak post-NACRT for predicting postoperative morbidity were 10.7 and 16.7 ([Formula: see text] at θ^L - AUC = 0.72, 77% sensitive and 83% specific; [Formula: see text] at peak - AUC = 0.80, 85% sensitive and 83% specific).

CONCLUSION:

NACRT before major rectal cancer surgery significantly decreased physical fitness as assessed by CPET.

[Eur J Surg Oncol](#). 2014 Nov;40(11):1421-8. doi: 10.1016/j.ejso.2014.03.021. Epub 2014 Apr 12; West MA et al.

Wait-and-see treatment strategies for rectal cancer patients with clinical complete response after neoadjuvant chemoradiotherapy: a systematic review and meta-analysis

Abstract

Wait-and-see treatment strategies may benefit rectal cancer patients who achieve a clinical complete response (cCR) after neoadjuvant chemoradiotherapy (NCRT). In this study, we analyzed data from 9 eligible trials to compare the oncologic outcomes of 251 rectal cancer patients achieving a cCR through nonsurgical management approaches with the outcomes of 344 patients achieving a pathologic complete response (pCR) through radical surgery. The two patient groups did not differ in distant metastasis rates or disease-free and overall survival, but the nonsurgical group had a higher risk of 1, 2, 3, and 5-year local recurrence. Hence, we concluded that for rectal cancer patients achieving a cCR after NCRT, a wait-and-see strategy with strict selection criteria, an appropriate follow-up schedule, and salvage treatments achieved outcomes at least as good as radical surgery. Long-term randomized and controlled trials with more uniform inclusion criteria and standardized follow-up schedules will help clarify the risks and benefits of wait-and-see treatment strategies for these patients.

[See comment in PubMed Commons below Oncotarget](#). 2016 Apr 6. doi: 10.18632/oncotarget.8622. [Epub ahead of print]; Li J et al.

Local excision of low rectal cancer treated by chemoradiotherapy: is it safe for all patients with suspicion of complete tumor response?

Abstract

PURPOSE:

The purpose of this study is to assess if local excision (LE) could be proposed if suspicion of complete tumor response (CR) after neoadjuvant chemoradiotherapy (CRT) for low rectal cancer (LRC) and this despite a potential risk of nodes (N+) or other tumor deposits (OTD) left in place. The aim was to assess in patients with LRC treated by CRT: (a) pathologic results of LE and total mesorectal excision (TME) in case of preoperative suspicion of CR and (b) the risk of N+ or OTD on TME if ypT0-Tis-T1 tumor.

PATIENTS:

Among 202 patients with LRC after CRT, 33 (16 %) with suspicion of CR underwent LE (n = 20) because of comorbidities and/or indication of definitive stoma or TME (n = 13). Pathologic examination of LE and TME specimens and oncological outcomes were assessed. Furthermore, 40/202 patients with pathologic CR on TME specimen (ypT0-Tis-T1) were assessed for possible N+ or OTD.

RESULTS:

In the 33 patients with suspicion of CR: (a) after LE, tumor was ypT0-Tis-T1 in only 15/20 cases (75 %); (b) after TME, tumor was ypT0-Tis-T1 in only 7/13 cases (54 %). Among 40 patients with ypT0-Tis-T1 tumor on TME specimen, 4 (10 %) presented N+ and/or OTD.

CONCLUSION:

In LRC with suspicion of CR after CRT, LE deserves a word of caution: 25 % of patients have in fact ypT2-T3 tumors. Furthermore, in patients with ypT0-Tis or T1 on TME specimen, a 10 % risk of N+ and/or OTD is observed. Thus, patient with suspicion of CR after CRT and treated by LE is exposed to a possible incomplete oncologic treatment.

[Int J Colorectal Dis.](#) 2016 Apr;31(4):853-60. doi: 10.1007/s00384-016-2546-1. Epub 2016 Mar 7; Debove C et al.

Oncological outcomes of local excision compared with radical surgery after neoadjuvant chemoradiotherapy for rectal cancer: a systematic review and meta-analysis

Abstract

BACKGROUND:

Low rectal cancer is conventionally managed with neoadjuvant chemoradiotherapy (CRT) followed by radical surgery (RS). In patients who refuse a stoma or are unfit for RS, an alternative approach may be the use of pre-op CRT and local excision (LE) where tumours are responsive. The aim of this systematic review is to determine whether differences exist in local recurrence (LR), overall survival (OS) and disease-free (DFS) survival between patients treated with CRT + LE and CRT + RS.

METHODS:

A literature search was performed using MEDLINE/PubMed/Ovid databases and Google Scholar between 1946 and 2013. Studies comparing outcome following LE and RS post-CRT were included. A pooled analysis was carried out using the Mantel-Haenszel statistical (random effects) model to identify differences in LR, OS and DFS between CRT + LE and CRT + RS.

RESULTS:

Eight studies were suitable for pooled analyses of LR whereas five and four studies were analysed for OS and DFS, respectively. When RS was used as the reference group, LR rate was higher in the LE group. However, this was non-significant (odds ratio (OR) 1.29, confidence interval (CI) 0.72-2.31, $p = 0.40$). Similarly, no difference was observed in 10-year OS (OR 0.96, CI 0.38-2.43, $p = 0.93$) or 5-year DFS (OR 1.04, CI 0.61-1.76, $p = 0.89$). There was evidence of publication bias in studies used for DFS. Subgroup analysis of above outcomes in T3/any N stage cancers showed no difference in LE versus RS.

CONCLUSION:

In the current evidence synthesis, there was no statistical difference in the LR, OS and DFS rates observed between patients treated with LE and RS for rectal cancer post-CRT. LE post-CRT may represent a viable alternative to RS for some patients wishing to avoid RS. However, further randomised studies are required to confirm these results.

[Int J Colorectal Dis.](#) 2015 Jan;30(1):19-29. doi: 10.1007/s00384-014-2045-1. Epub 2014 Nov4; Shaikh I. et al.

[Impact of neoadjuvant radiochemotherapy on erectile and urinary functions in mid-low rectal cancer patients: A prospective non-randomized controlled trial]

Abstract

OBJECTIVE:

To study the impact of neoadjuvant radiochemotherapy on erectile and urinary functions in mid-low rectal cancer patients.

METHODS:

Seventy mid-low rectal cancer patients from January 2012 to May 2013 in The Sixth Affiliated Hospital, Sun Yat-sen University were prospectively enrolled. According to tumor staging and patient decision, patients received neoadjuvant radiochemotherapy (50 Grays administered over a six-week period and four cycles of concomitant mFOLFOX6 chemotherapy followed by operation (study group) or surgery alone (control group). Dropouts, loss to follow up and relapse during follow-up were removed from the analysis. A total of 30 patients stayed in study group and 29 patients in control group. To assess erectile and urination functions, the five-item version of the international index of erectile function (IIEF-5) and the international prostate symptom score (IPSS) questionnaires were used before therapy and 12 months after surgery.

RESULTS:

In both study and control groups, total IIEF-5 score was decreased significantly at postoperative 12-month compared to initial assessment ($P < 0.01$). Compared with control group, IIEF-5 score change was significantly higher in study group (9.6 ± 6.1 vs. 5.3 ± 5.3 ; $P < 0.01$). Total IPSS score in both groups was increased significantly at postoperative 12-month compared to initial assessment ($P < 0.05$). No significant difference was found in IPSS score change between the two groups (3.0 ± 3.4 vs. 1.5 ± 3.0 , $P > 0.05$). Univariate analysis on study group showed that age, tumor location and maximal diameter were associated with erectile dysfunction. Age was associated with urination dysfunction (all $P < 0.05$).

CONCLUSION:

Neoadjuvant radiochemotherapy has significant impact on erectile dysfunction after surgery in mid-low rectal cancer patients.

[See comment in PubMed Commons below Zhonghua Wei Chang Wai Ke Za Zhi. 2016 Jan;19\(1\):45-9; Wang J. et al.](#)

Timely tumor response analysis after preoperative chemoradiotherapy and curative surgery in locally advanced rectal cancer: A multi-institutional study for optimal surgical timing in rectal cancer

Abstract

BACKGROUND AND PURPOSE:

The definite surgical timing in rectal cancer after preoperative chemoradiotherapy (CRT) has not yet been fully examined. We assess the tumor response and identify the optimal operation timing after preoperative CRT in rectal cancer.

METHODS AND MATERIALS:

The study included data of 1786 patients with locally advanced rectal cancer (cT3-4N0-2M0). They received preoperative CRT followed by total mesorectal excision. Total radiation dose was 50.4Gy in 28 fractions. Interval time between preoperative CRT and surgery ranged from 2 to 26weeks, with a median interval of 7.2weeks. Primary endpoint was to evaluate the period of highest downstaging and pathological complete response (ypCR) rates to determine the optimal timing for curative surgery after CRT.

RESULTS:

Downstaging rates peaked between 6 and 7weeks after CRT and declined afterward. ypCR rates increased from 5 to 6weeks after CRT and decreased after 9 to 10weeks. Downstaging rates were similar between the two arms showing 36.9% in the early arm (≤ 7 weeks) and 37.0% in the delayed arm (> 7 weeks). ypCR rates were significantly higher in the delayed arm, as compared to the early arm (12.3% vs. 8.6%, $p=0.011$). The delayed arm had higher sphincter preservation rates than the early arm with a marginal significance (92.4% vs. 89.9%, $p=0.078$). There was no statistically significant difference regarding relapse-free survival and overall survival between the two arms.

CONCLUSIONS:

ypCR rates increased after 5weeks and decreased after 10weeks and the delayed (> 7 weeks after CRT) group showed significantly increased ypCR rates than the early arm (≤ 7 weeks after CR). The optimal timing for curative surgery in rectal cancer when tumor response is maximal is after 7weeks and before 10weeks following preoperative CRT.

[Radiother Oncol](#). 2016 Apr 19. pii: S0167-8140(16)31024-6. doi: 10.1016/j.radonc.2016.03.017. [Epub ahead of print]; Kwak YK et al.



Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden



Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden



Neoadjuvante Radiotherapie
Vollremission bis Langzeitschaden

