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Munich Masterclass Pankreas-Ca

Radioonkologie

Klinik für Strahlentherapie, LMU Klinikum
25.9.2020 | Prof. Dr. med. Dipl.-Phys. Maximilian Niyazi

Forschungsunterstützungen

Unserer Rolle als Universitätsklinik entsprechend sind wir forschungsaktiv und erhalten dazu Zuwendungen von diversen Seiten

Forschung wird unterstützt von staatlichen Stellen: Freistaat Bayern, Krebshilfe, DFG, BMBF (DKTK, DZL) und BMU

Für einzelne Forschungsprojekte und/oder Kongresspräsentationen sowie die Teilnahme an Advisory-Boards wird die Klink unterstützt von:

AstraZeneca, MERCK, MSD, BMS, ViewRay, ELEKTA, Brainlab und C-RAD und OPASCA

Klinik für Strahlentherapie
LMU München

LMU KLINIKUM

2400 Patienten /Jahr

Ausstattung

2 Elekta Versa HD
mit Brainlab Exac Trac
3 Elekta Synergy mit Agility MLC
1 x Clarity
2 x C-Rad Catalyst
1 ViewRay MRIdian
Brachytherapie Elekta Fexitron Afterloader

Personal

32 Ärzte (9 Oberärzte, 23 Assistenten)
22 Medizinphysiker/Techniker
10 Biologen
23 RTAs

Adjuvante RCHT vs Beobachtung vs ChTx

- Unzählige alte Studien mit inkongruenten Ergebnissen, z. B.:
  - GITSG
  - EORTC
  - RTOG
  - ESPAC

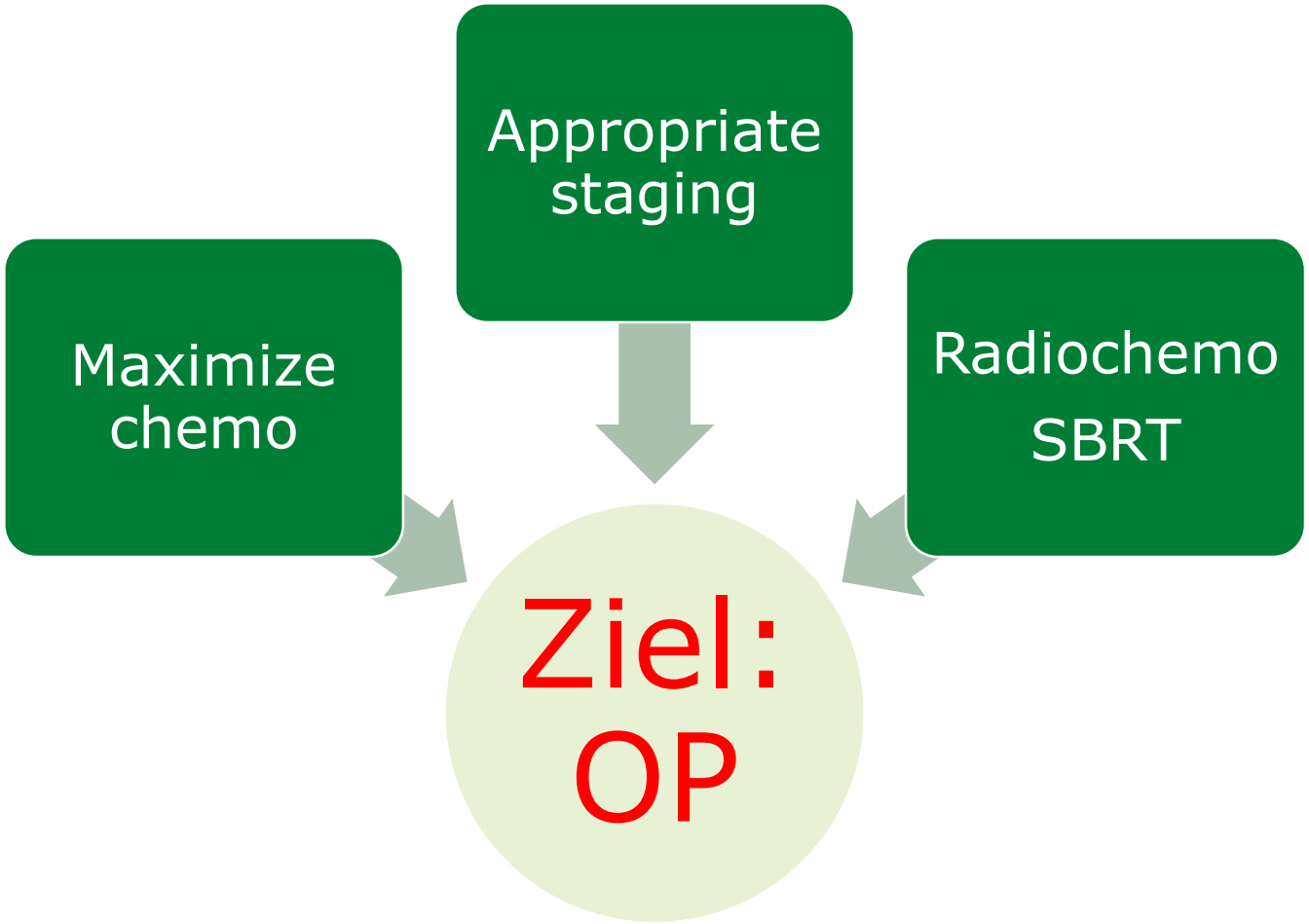
PROBLEM:

veraltete RT Technik, inadäquate Dosis/Fraktionierung

(split course), veraltete systemische Therapien
→ nur von historischem Wert

Hohe Tox

Ziel der Neoadjuvanz



RT/RCX:

- ✓ Tumorverkleinerung
- ✓ Verbesserung der Resektabilität
- ✓ Palliative RT zur lokalen Symptomkontrolle (Schmerzen)
- ✓ Progressionsfreies Intervall verlängern

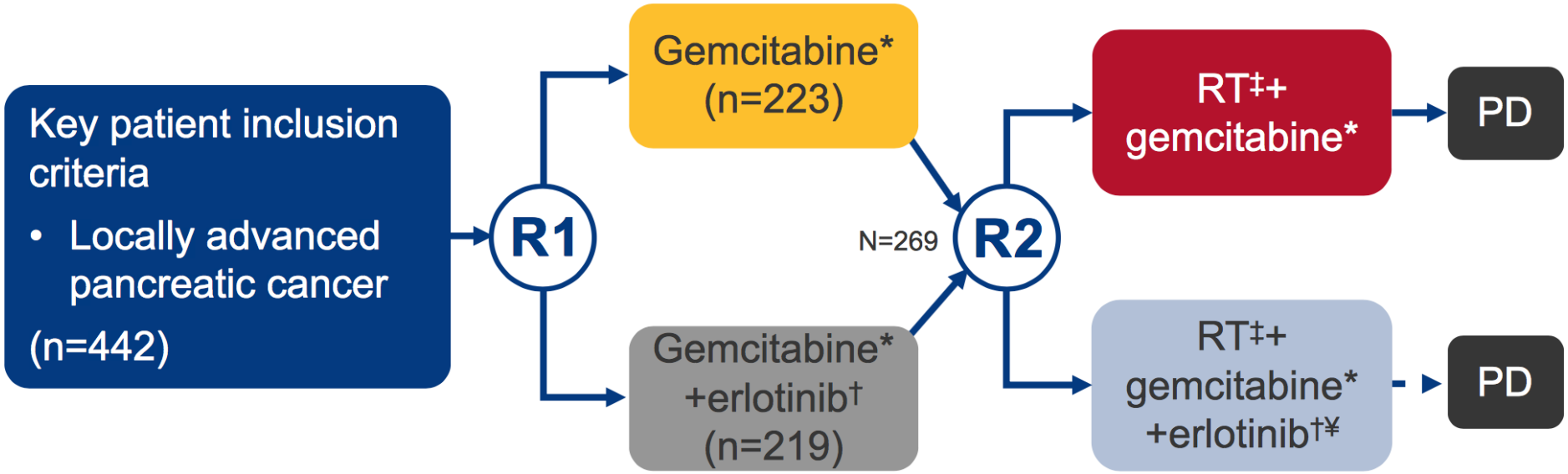
Neoadjuvante Therapie – lokal fortgeschrittene tumore

- Studien Chemo +/- RT

		Mediane ÜLZ (Monate)	
ECCOG 4201-Studie inoperable Tumoren	**RCT → CT**	**11,1**	**P = 0,017**
	CT	**9,2**	
Ioka et al. 2010 inoperable Tumoren	**RCT → CT**	**13**	**P = 0,02**
	CT	**12,4**	
GERCOR: Phase II/III-Studie inoperable Tumoren	**CT → RCT**	**15,0**	**P = 0,0009**
	CT	**11,7**	
FFCD/SFRO-Studie inoperable Tumoren	**RCT → CT**	**8,6**	**P = 0,03**
	CT	**13**	
LAP 07-Studie	**CT → RCT** **CT**	**15,2** **16,5**	**P = 0,8**

LAP07 Studie

- **Study objective**
  - To determine whether OS is improved with CRT in patients with locally advanced pancreatic cancer whose tumour is controlled after 4 months of induction CT



Primary endpoint

- OS

Secondary endpoints

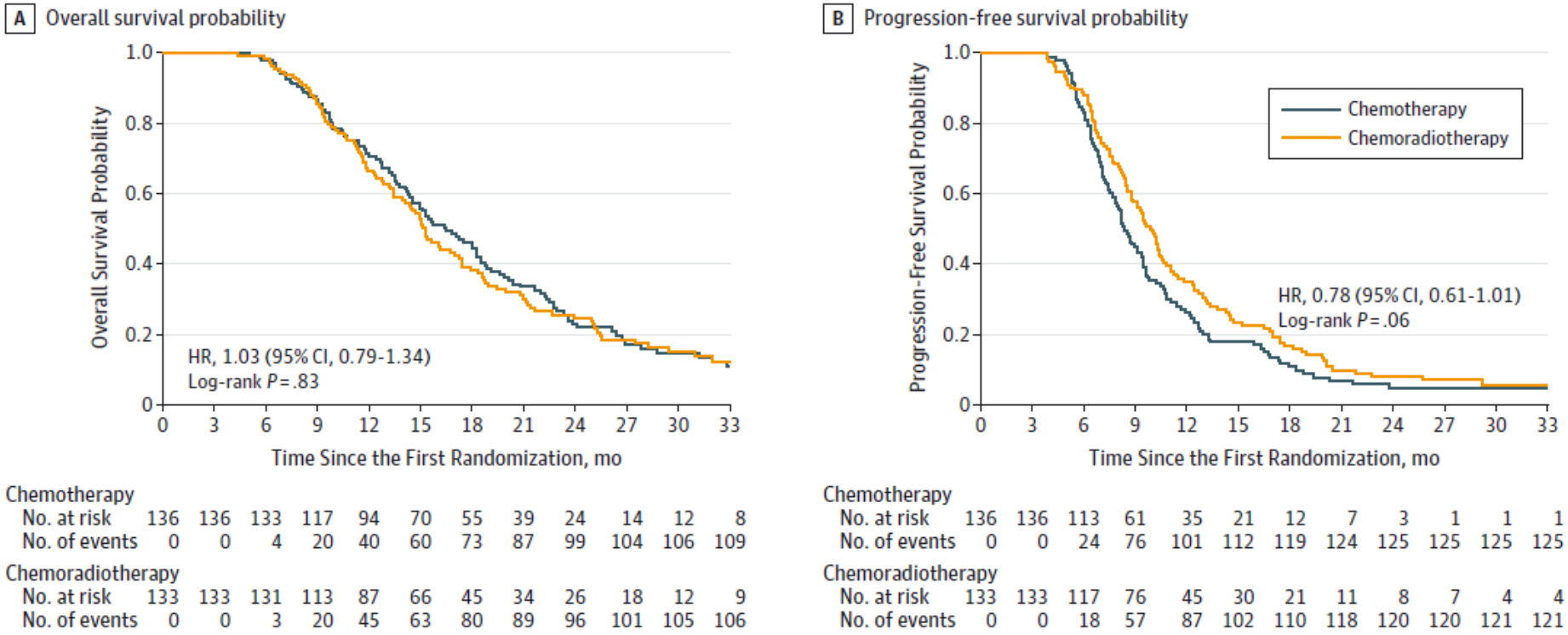
- PFS and tolerance

*1000 mg/m²/wk x3; †100 mg/day; ‡54 Gy (5x 1.8 Gy/day) + capecitabine 1600 mg/m²/day; ¥150 mg/day maintenance

Huguet et al. J Clin Oncol 2014; 32 (suppl 5; abstr 4001)

LAP07 Studie

Figure 3. Kaplan-Meier Curves of Overall Survival and Progression-Free Survival, According to the Second Randomization



Chemotherapy												
No. at risk	136	136	133	117	94	70	55	39	24	14	12	8
No. of events	0	0	4	20	40	60	73	87	99	104	106	109
Chemoradiotherapy												
No. at risk	133	133	131	113	87	66	45	34	26	18	12	9
No. of events	0	0	3	20	45	63	80	89	96	101	105	106

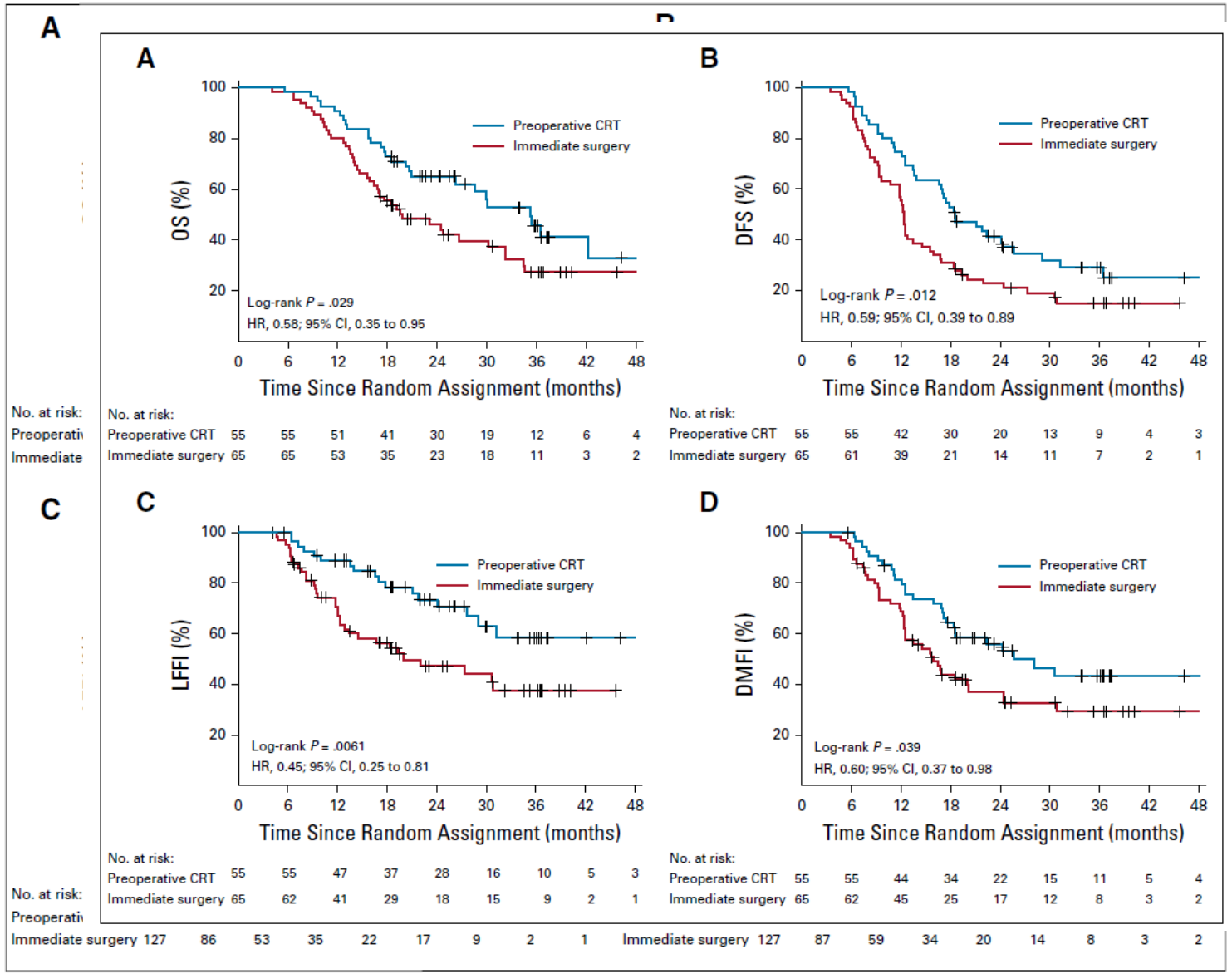
Chemotherapy												
No. at risk	136	136	113	61	35	21	12	7	3	1	1	1
No. of events	0	0	24	76	101	112	119	124	125	125	125	125
Chemoradiotherapy												
No. at risk	133	133	117	76	45	30	21	11	8	7	4	4
No. of events	0	0	18	57	87	102	110	118	120	120	121	121

Hammel P et al, JAMA 2016; 315: 1844

➢ Bessere lokale Kontrolle

Neoadjuvante Therapie – (borderline)resektable tumore

original reports



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esten, MD, PhD[10];
Homs, MD, PhD[9];

ngen, MD, PhD[20];
), PhD[22];

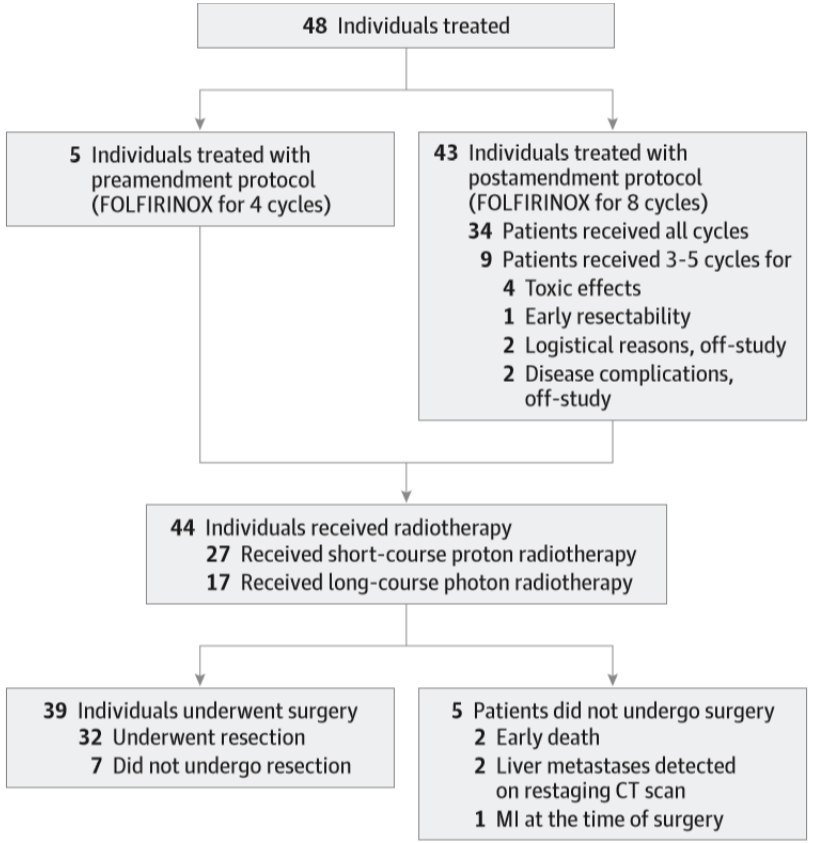
DPCG 4
eatic Cancer Group

JAMA Oncology | Original Investigation

Total Neoadjuvant Therapy With FOLFIRINOX Followed by Individualized Chemoradiotherapy for Borderline Resectable Pancreatic Adenocarcinoma

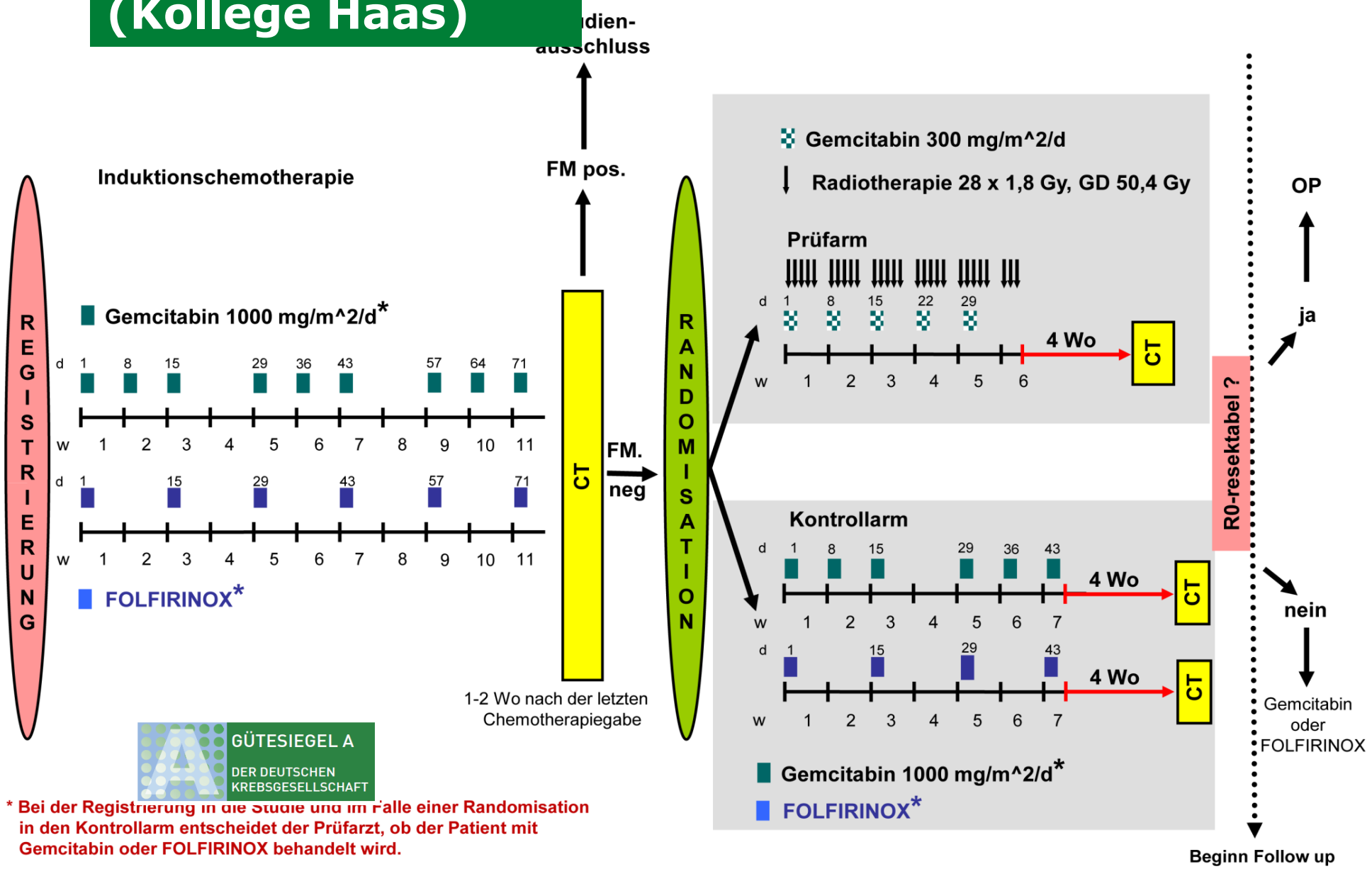
A Phase 2 Clinical Trial

Patientenzahl	N=48
Short course CRT	27 / 48 (56%)
Konvent. CRT	17 / 48 (35%)
R0	**31 / *32* (97%)**
mPFS (all)	**14.7 mo**
mPFS (resection)	**48.6 mo**



Murphy JE et al, JAMA Oncol 2018; 4: 963

CONKO-007 Studie (Kollege Haas)



GÜTESIEGEL A
DER DEUTSCHEN KREBSGESELLSCHAFT

* Bei der Registrierung in die Studie und im Falle einer Randomisation in den Kontrollarm entscheidet der Prüfarzt, ob der Patient mit Gemcitabin oder FOLFIRINOX behandelt wird.

ASTRO Leitlinie

4. For patients with borderline resectable pancreatic cancer and select locally advanced pancreatic cancer appropriate for downstaging prior to surgery, a neoadjuvant therapy regimen of systemic chemotherapy followed by conventionally fractionated RT with chemotherapy is conditionally recommended.	**Conditional**	**Moderate**	**85%** *
5. For patients with borderline resectable pancreatic cancer and select locally advanced pancreatic cancer appropriate for downstaging prior to surgery, a neoadjuvant therapy regimen of systemic chemotherapy followed by multifraction SBRT is conditionally recommended.	**Conditional**	**Low**	**77%** *
6. For patients with locally advanced pancreatic cancer not appropriate for downstaging to eventual surgery, a definitive therapy regimen of systemic chemotherapy followed by either (1) conventionally fractionated RT with chemotherapy, (2) dose-escalated chemoradiation, or (3) multifraction SBRT without chemotherapy is conditionally recommended.	**Conditional**	**Low**	**85%** *
3. For patients with locally advanced pancreatic cancer selected for definitive conventionally fractionated or dose-escalated RT with chemotherapy, 5040-5600 cGy in 175-220 cGy fractions with concurrent chemotherapy is conditionally recommended.	**Conditional**	**Low**	**100%** †

ASTRO Leitlinie

4. For patients with borderline resectable pancreatic cancer selected for SBRT, 3000-3300 cGy in 600-660 cGy fractions with a consideration for a simultaneous integrated boost of up to 4000 cGy to the tumor vessel interface is conditionally recommended.	**Conditional**	**Moderate**	**100%**†
5. For patients with locally advanced pancreatic cancer selected for SBRT, 3300-4000 cGy in 660-800 cGy fractions is recommended.	**Strong**	**Moderate**	**100%**†

Konventionell vs. SBRT: Was ist besser?

Zhong et al.

Original Article

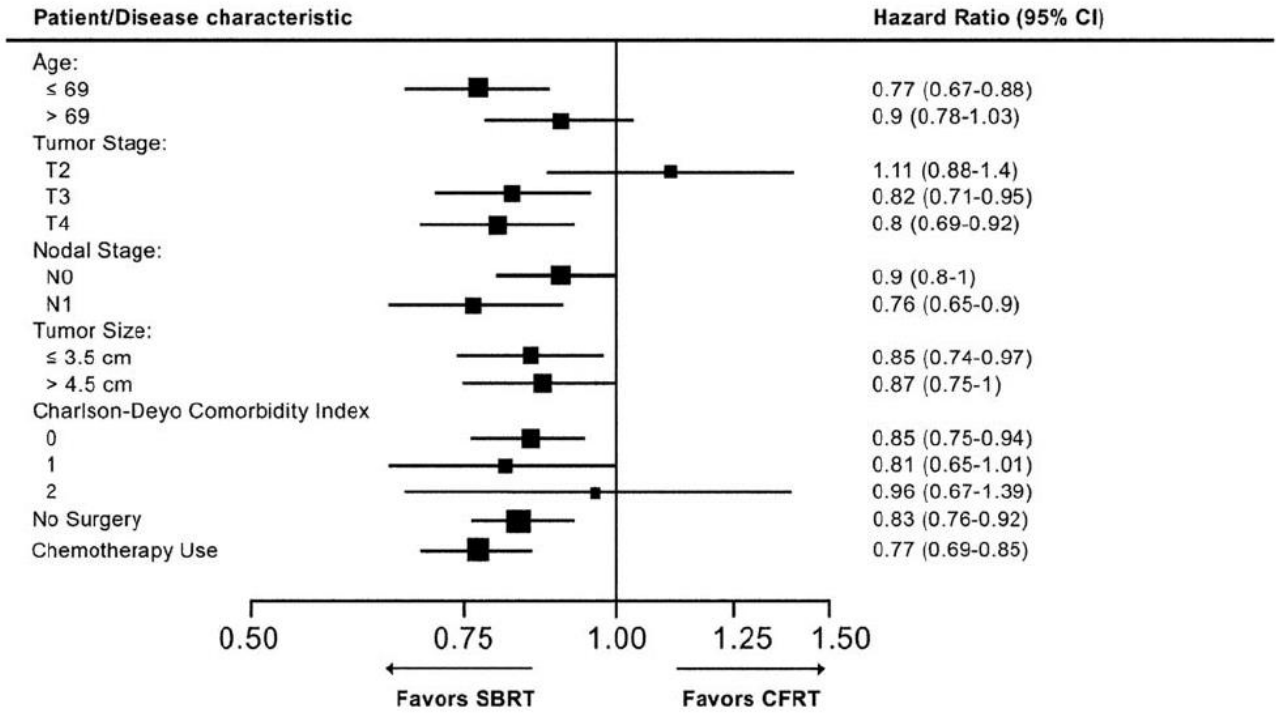


Figure 3. Multivariate subgroup analyses of the effects of patient demographics, disease characteristics, and treatment details on overall survival with CFRT versus SBRT. CI indicates confidence interval; CFRT, conventionally fractionated radiation therapy; SBRT, stereotactic body radiation therapy.

Datenlage SBRT-Dosis

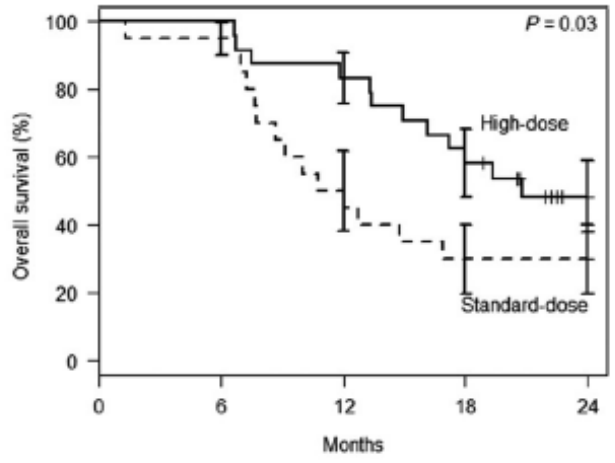


FIGURE 1 Overall survival from start of radiation therapy stratified by biologically effective dose (BED_{10}). Standard error bars displayed at each 6-mo timepoint

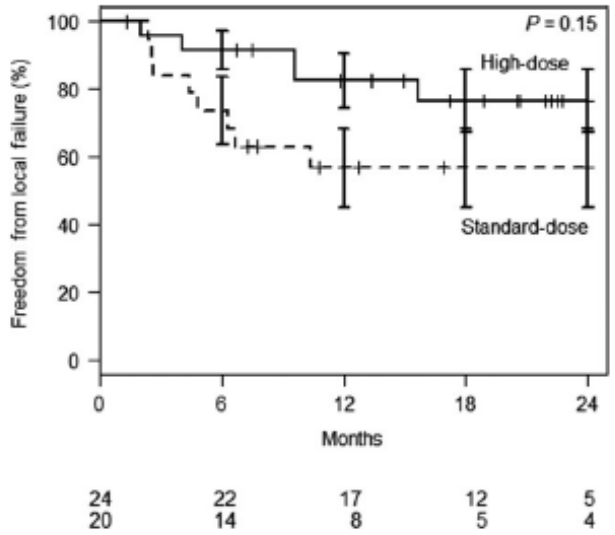


FIGURE 2 Freedom from local failure from start of radiation therapy stratified by biologically effective dose (BED_{10}). Standard error bars displayed at each 6-mo timepoint

Received: 5 January 2019 | Revised: 12 February 2019 | Accepted: 26 February 2019
DOI: 10.1002/cam4.2100

ORIGINAL RESEARCH

WILEY Cancer Medicine

Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer

Soumon Rudra[1] | Naomi Jiang[2] | Stephen A. Rosenberg[3] | Jeffrey R. Olsen[1] | Michael C. Roach[1] | Leping Wan[1] | Lorraine Portelance[4] | Eric A. Mellon[4] | Anna Bruynzeel[5] | Frank Lagerwaard[5] | Michael F. Bassetti[3] | Parag J. Parikh[1] | Percy P. Lee[2]

- N=44
- Primär inoperabel
- MRgRT
- Medianes F/U 17 Monate
- Keine G3+ Tox in der Hochdosisgruppe

Advances in Radiation Oncology (2020) xx, 1-8

advances in radiation oncology

www.advancesradonc.org

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5 x 10 Gy!?

Clinical Investigation

Ablative Five-Fraction Stereotactic Body Radiation Therapy for Inoperable Pancreatic Cancer Using Online MR-Guided Adaptation

Comron Hassanzadeh, MD, MPH,[a] Soumon Rudra, MD,[a] Ani Bommireddy, BA,[b] William G. Hawkins, MD,[c] Andrea Wang-Gillam, MD, PhD,[d] Ryan C. Fields, MD,[c] Bin Cai, PhD,[a] Justin Park, PhD,[a] Olga Green, PhD,[a] Michael Roach, MD,[e] Lauren Henke, MD,[a] and Hyun Kim, MD[a,*]

Table 1 Patient demographics and baseline characteristics

	All patients (n = 44)
Follow-up (median and range)	16 mo (7-52)
Age, year	
Median (range)	71 (42-93)
Sex, no. (%)	
Male	29 (66)
Female	15 (34)
ECOG performance status score, no. (%)	
0	12 (27)
1	20 (46)
2	9 (21)
3	2 (5)
Location of tumor, no. (%)	
Head	35 (80)
Body/tail	9 (20)
Proximity to OARs, no. (%)	
Abutting OAR	35 (80)
Invading OAR	5 (11)
No tumor involvement	4 (9)
Resectability at diagnosis, no. (%)	
Unresectable	28 (64)
Borderline resectable	6 (14)
Medically inoperable	10 (23)
Neoadjuvant chemotherapy, no. (%)	
FOLFIRINOX	16 (36)
Nab-paclitaxel and gemcitabine	15 (34)
Gemcitabine alone	3 (7)
Nab-paclitaxel alone	2 (4)
No neoadjuvant	8 (18)
Radiation modality, no. (%)	
Cobalt-60 system	38 (86)
MR-LINAC system	6 (14)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; MR-LINAC = magnetic resonance-guided linear accelerator; OAR = organs-at-risk.

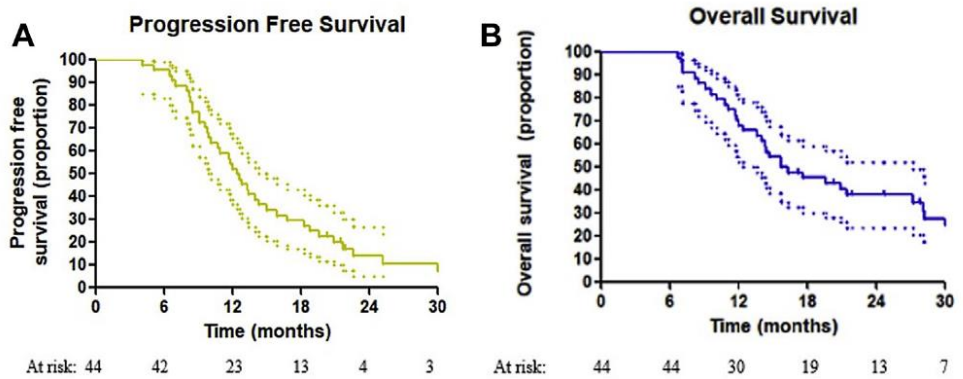
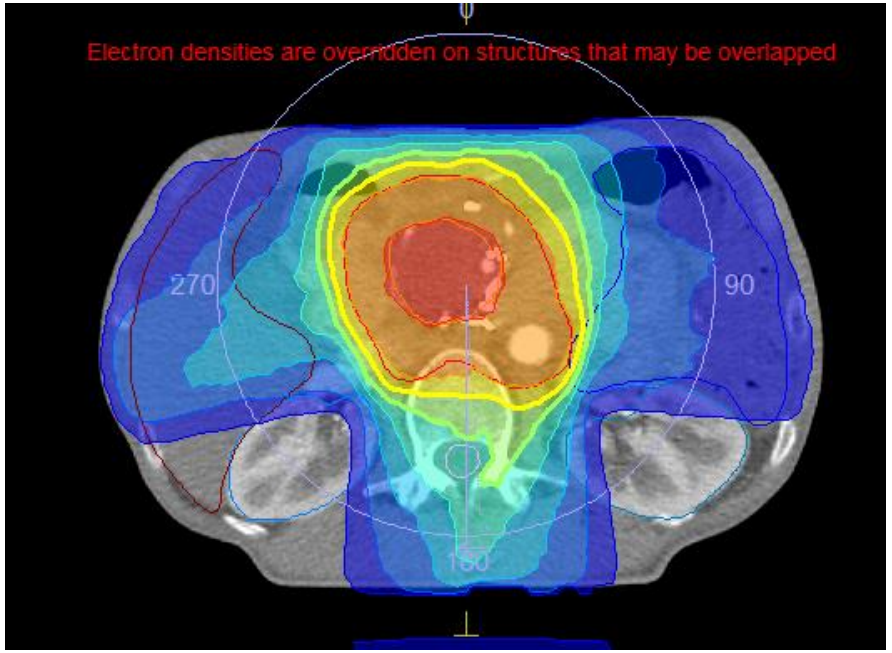


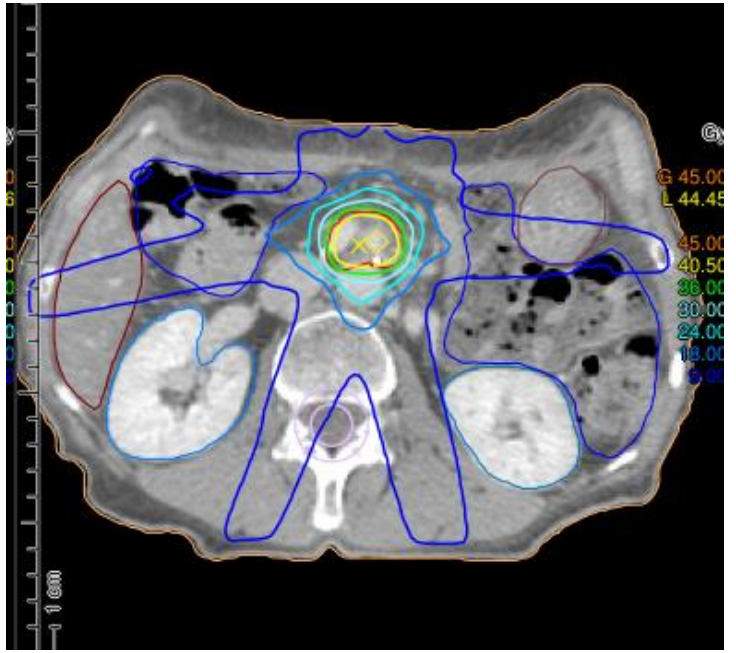
Figure 3 Kaplan-Meier estimates of survival for (A) progression-free survival and (B) overall survival. The 95% confidence intervals are included as dotted lines.

- N=44, LAPC
- Primär inoperabel
- MRgRT („SMART“)
- Medianes F/U 16 Monate
- 4,6% G3, 6,8% G2 Tox
- Medianes OS 15,7 Monate

Neue Techniken Strahlentherapie



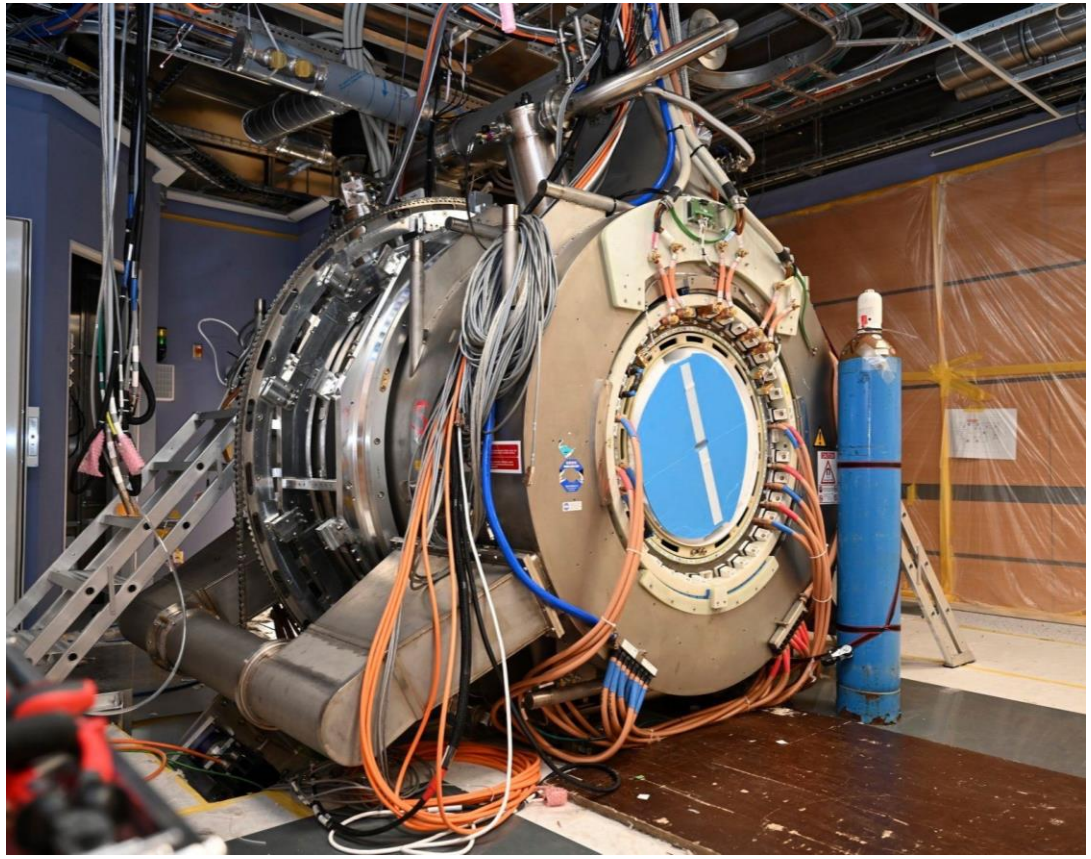
vs

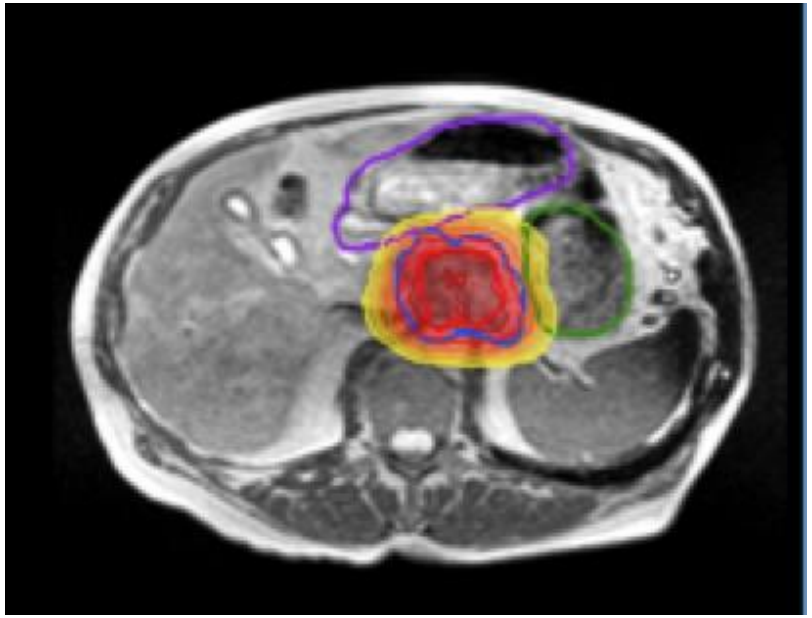


kombinierte klassische Radiochemotherapie mit Gemcitabine, SIB 55/ 45 Gy

Stereotaktische Bestrahlung
3x 12 Gy (80% isodose)
~ 66-94 Gy
konv. Fraktionierung

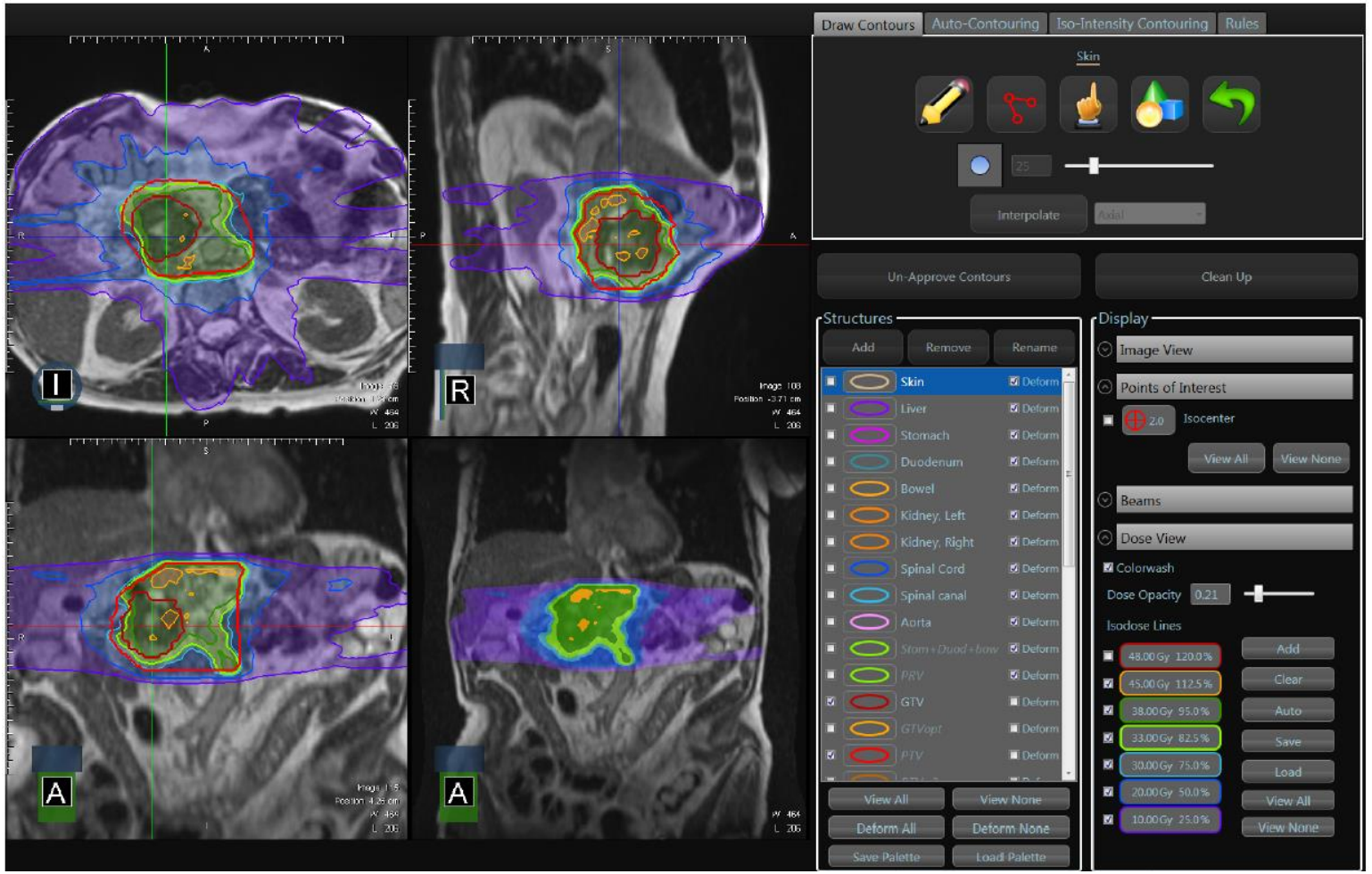
SBRT – MR linac





Luterstein et al, Cureus 2018

Männlich, 79 Jahre - Pankreas Ca mit LAW



04/2020: 3x8Gy / Woche ad 40Gy GD, 80% Isodose Pankreas CA inkl. LAW

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MASPAC-Studie

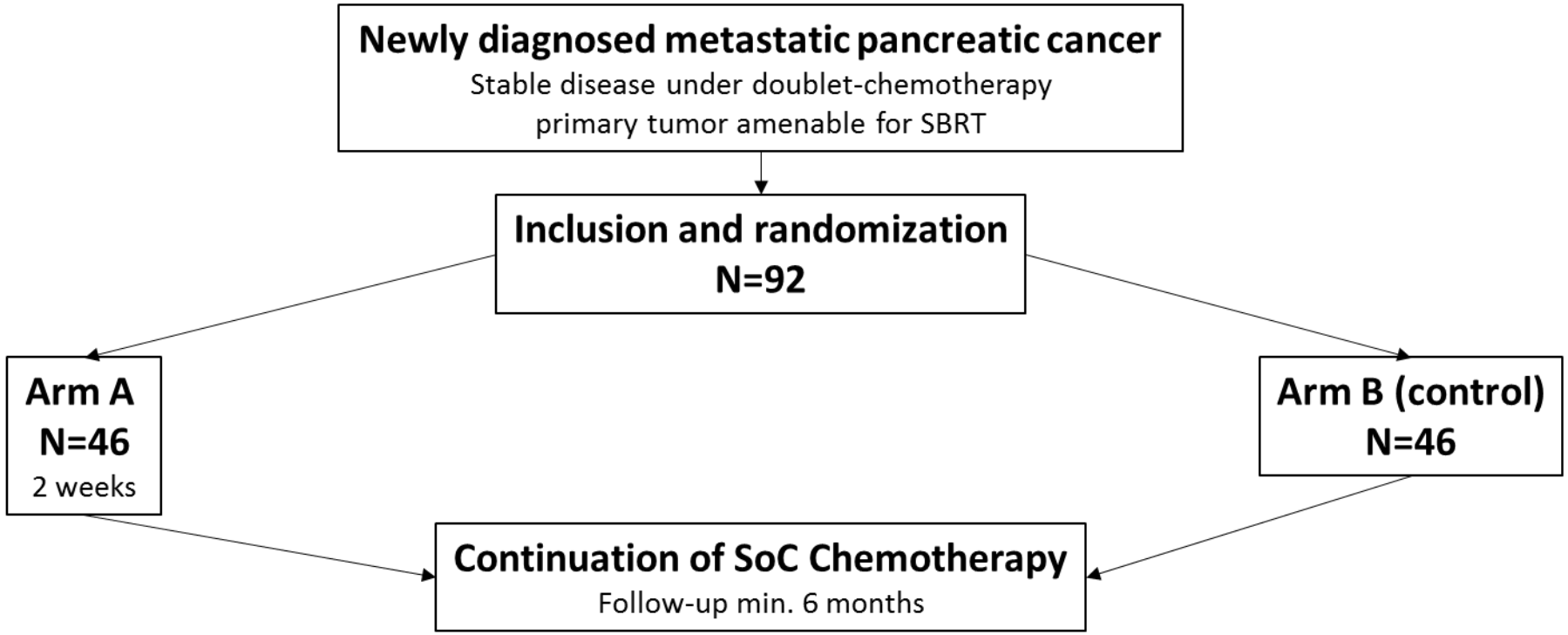
Nahe Zukunft/1/2021

MR-Guided Adaptive Stereotactic Body Radiotherapy (SBRT) of Primary Tumor for Pain Control in Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC) – a Randomized, Controlled Clinical Study

MASPAC-Studie
Nahe Zukunft/1/2021

- Multizentrische Studie des deutschsprachigen MRIdian-Konsortiums (Heidelberg, Zürich, LMU München)
- Randomisierte Studie
- Einschlusskriterium: erwachsene Patienten mit PDAC bis ECOG2, welche nach 2 Monaten einer Standardchemotherapie nicht progredient waren; zusätzlich keine Ausschlusskriterien für eine Behandlung am MR-Linac
- N = 92 geplant
- Primärer Endpunkt: Mean kumulativer Pain Index

MASPAC-Studie
Nahe Zukunft/1/2021



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Ganz herzlichen Dank Ihnen!

Fragen?