VLOGA RADIOTERAPIJE PRI RAKU JAJČNIKOV

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IZ SMERNIC, 2015

OBSEVANJE

- kot paliativno zdravljenje v primeru metastatske bolezni z namenom lajšanja simptomov (krvavitev, bolečina, dispneje, možganski zasevki, ipd.)
- kot »reševalno obsevanje« v primeru lokaliziranega ostanka bolezni:
  - po primarnem zdravljenju s kirurgijo in kemoterapijo
  - ob lokalizirani ponovitvi bolezni, ko kirurško zdravljenje ni možno
  - po nepopolni sekundarni citoredukciji

2015 VS 2020

	2015 OI	2020 OI	2020 UKC MB
Skupaj	35	25	6
medenica (vključena krvavitev iz nožnice)	17	10	1
bezgavke nad prepono	5	2	1
bezgavke pod prepono	5	1	0
kožni zasevki	3	0	1
skelet	3	8	2
možganski zasevki	2	2	1
trebuh	0	2	0

Paliativno obsevanje 17 / 25 (+ UKC MB 6 / 6)

- 1 – 10 frakcij
- TD 8 – 30 Gy

Obsevanje z veliko dozo 5 / 25

- 12 - 25 frakcij
- TD 36 – 50 Gy

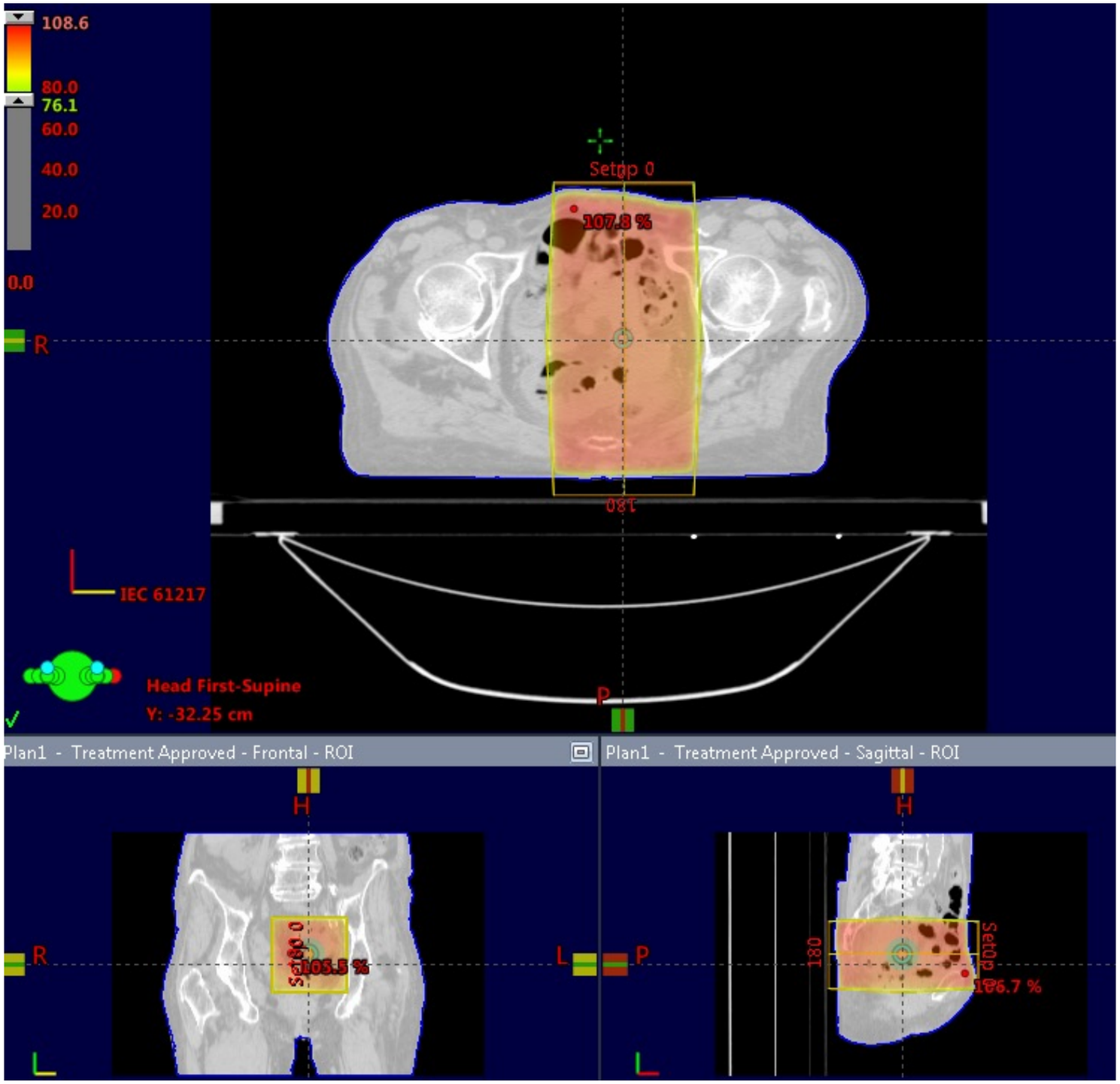
SBRT / SRS 3 / 25

- 1 – 5 frakcij
- Velike doze na frakcijo (22,5 Gy, 16 Gy, 8 Gy) in TD

PALIATIVNO OBSEVANJE

- Veliko izkušenj, številne raziskave
- Bolnice z napredovalo boleznijo
- namen: lajšanje simptomov (bolečina, krvavitev iz nožnice, težko dihanje, simptomi zaradi možganskih zasevkov, pritiska povečanih bezgavk)
- Malo število obsevanj, majhne doze
- Choan, 2006: CR zmanjšanje bolečine 65 %, zaustavitev krvavitve 88 % (CR + PR 100 %)
- Jiang, 2018: CR + PR: zmanjšanje bolečine 87 % (skeletne le 75 %), zaustavitev krvavitve 93 %

PALIATIVNO OBSEVANJE



OBSEVANJE Z VELIKO DOZO

- Večje število frakcij, velika skupna doza
- Različno poimenovanje glede na to, kdaj se odločimo za obsevanje / namen in tehnika obsevanja enaki
- Reševalno – konsolidacijsko - pooperativno – radikalno
- Lokalizirana bolezen

Lokaliziran ostanek po primarnem zdravljenju

Lokalizirana inoperabilna ponovitev

Lokalizirana ponovitev (z nepopolno citoredukcijo) R1, R2

- Ob operaciji označba sumljivih mest s klipi (naleganje na žile, obraščanje sečevoda)
- Namen: zmanjšanje tumorske formacije (delni ali popolni odgovor), izboljšanje lokalne kontrole bolezni

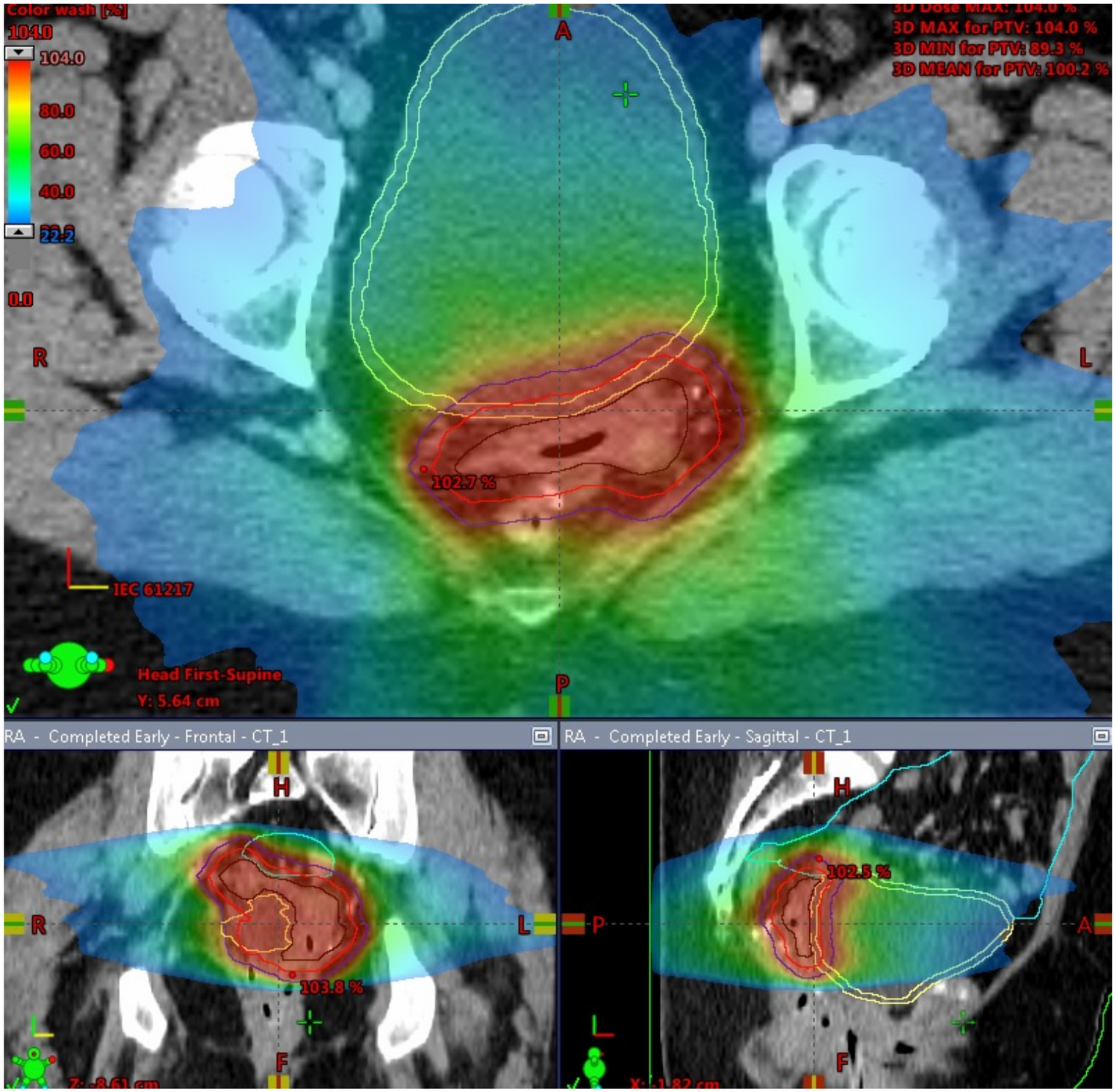
OBSEVANJE Z VELIKO DOZO

- Lokaliziran recidiv, 60 – 62 % citoredukcija pred RT
- TD 45 - 60 Gy (Yahara, 2013, Brown, 2013)
- Izboljšanje lokalne kontrole (LC 90 %), daljši čas do progresa (> 1 leto), ponovne KT, boljši OS
- Večina novih ponovitev izven RT polja
- Smart, 2019: 10 % po 5-ih letih brez ponovitve bolezni

Author	Year	Stage	Study design	N	Comments
Albuquerque *et al.* (54)	2016	Nodal, pelvis Retroperitoneal	Retrospective IFRT median dose: 50 Gy conventional fractionation	27	5-year LRFS: 70%; 5-year DFS: 33%
Choi *et al.* (55)	2017	Nodal and extranodal disease	3D-CRT	44	The 1- and 2-year in-field LC rates were 66.0% and 55.0%, respectively. BED ≥50 Gy showed better outcomes
Chang *et al.* (56)	2018	Nodal and extranodal disease	Prospective phase II; IFRT-IMRT, 3D-CRT or brachytherapy	–	Overall and CRRs were 85.7% and 50%, respectively. The 2-year PFS rate was 39.3%. The 3-year LC and OS rates were 84.4% and 55.8%, respectively
Komura *et al.* (57)	2019	Nodal or extranodal recurrence	Retrospective 3D-CRT	24	In-field overall response of 58.3%, median regression was 40.2%. The 1-year survival and local PFS rates after RT were 66.7% and 45.8%, respectively
Smart *et al.* (58)	2019	Peritoneal, nodal, vaginal	Retrospective IFRT 3D-CRT	40	At 3 years, DFS and OS were 18% and 80%, respectively. Non-serous histology and platinum sensitivity were associated with lower relapse risk

Flores-Balcázar and Urías-Arce. RT in women with epithelial OC

OBSEVANJE Z VELIKO DOZO



SBRT / SRS

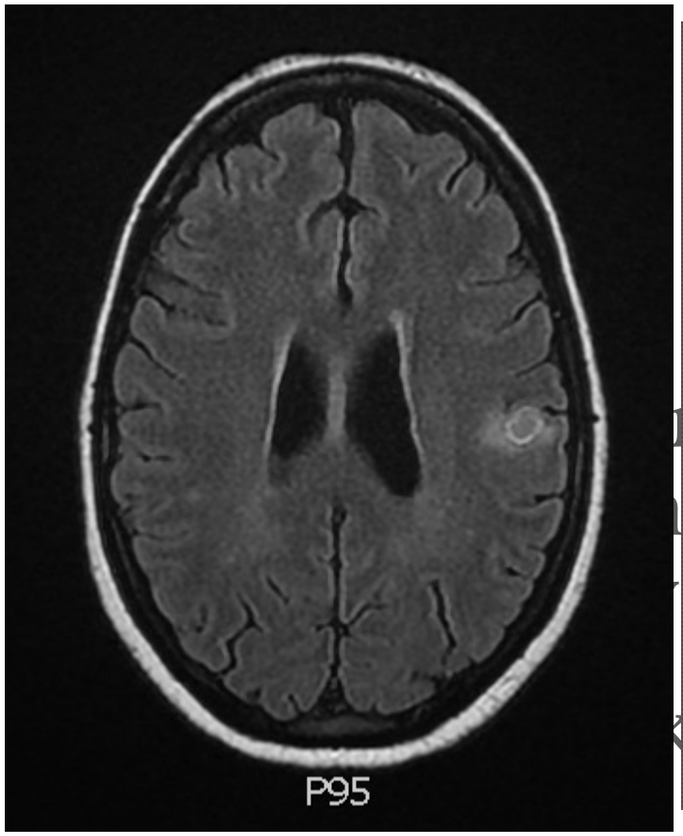
- Prve bolnice z rakom jajčnika na OI 2020
- Solitarni zasevek
- Lega, velikost, v katerem organu, prileţne strukture dobro omejena lezija, PS po WHO

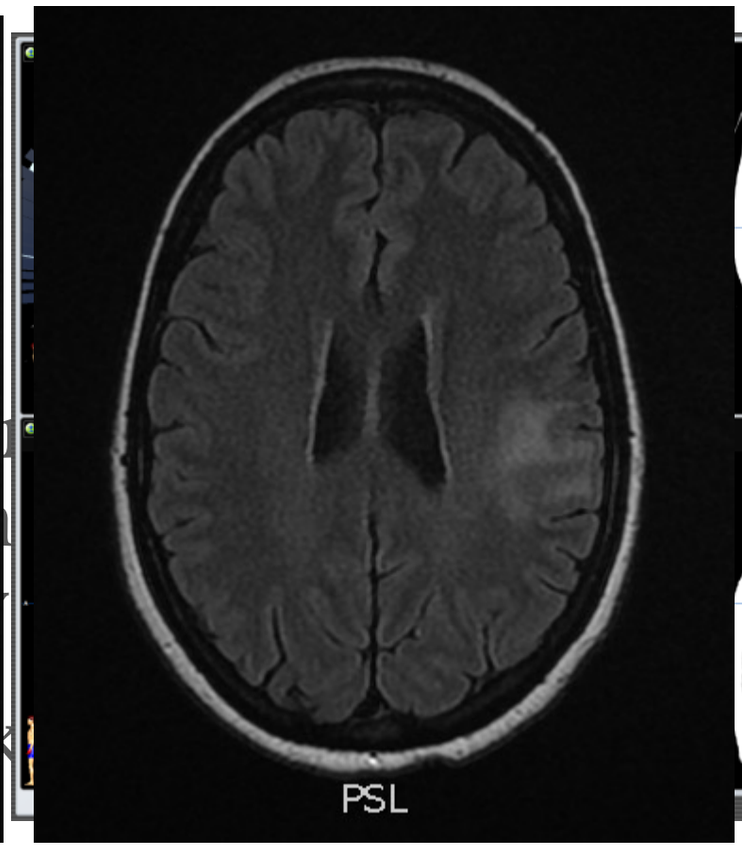
- 3 bolnice (1 bolnica s solitarnim zasevkom v CŽS, 2 bolnici s solitarnim zasevkom v jetrih)

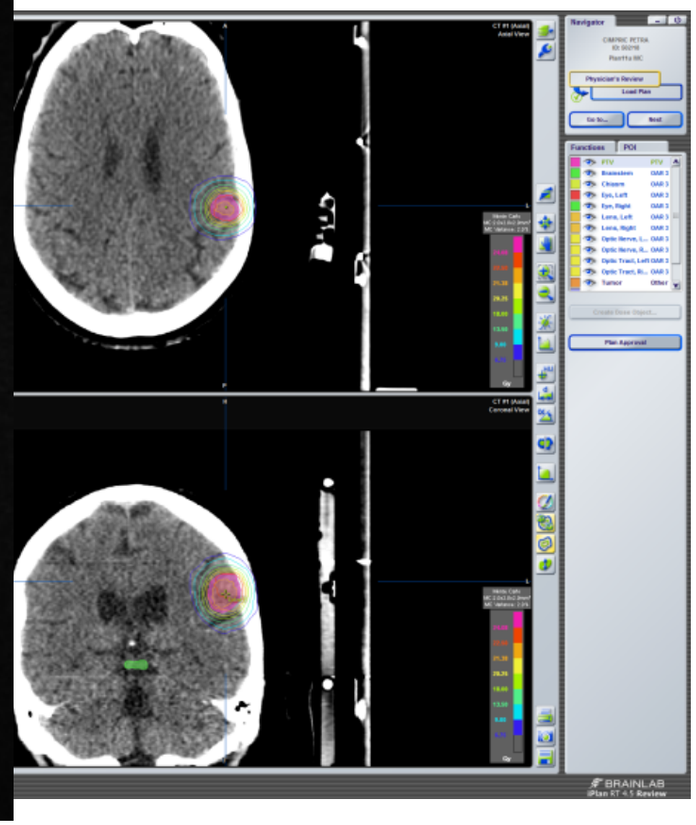
Author	Year	Study design	N	Comments
Iftode *et al.* (68)	2018	Retrospective SBRT (lymph nodes, liver, lung)	26 patients; 44 lesions	1-year PFS: 69.3%, 1-year OS: 100%; 2-year PFS: 38%, 2-year OS: 92.7%; 5-year PFS: 19%, 5-year OS: 61.7%
Lazzari *et al.* (69)	2018	Retrospective SBRT	82 patients; 156 lesions	Median systemic treatment-free interval after SBRT: 7.4 months, 2-year local PFS: 68%, PFS: 18%, OS: 71%.
Macchia *et al.* (70)	2020	Retrospective, multicenter study (MITO RT-01) SBRT/SRS	261 patients; 449 lesions	CRR: 65.2%, PRR: 23.8%, SD: 7.4%, PD: 3.6%; 2-year LC: 81.9%, ORR: 89%, CB: 96.4%, AT: 20.7%, LT: 6.1%, 2-year late TFS: 95.1%

Flores-Balcázar and Urías-Arce. RT in women with epithelial OC

PRIMER SRS

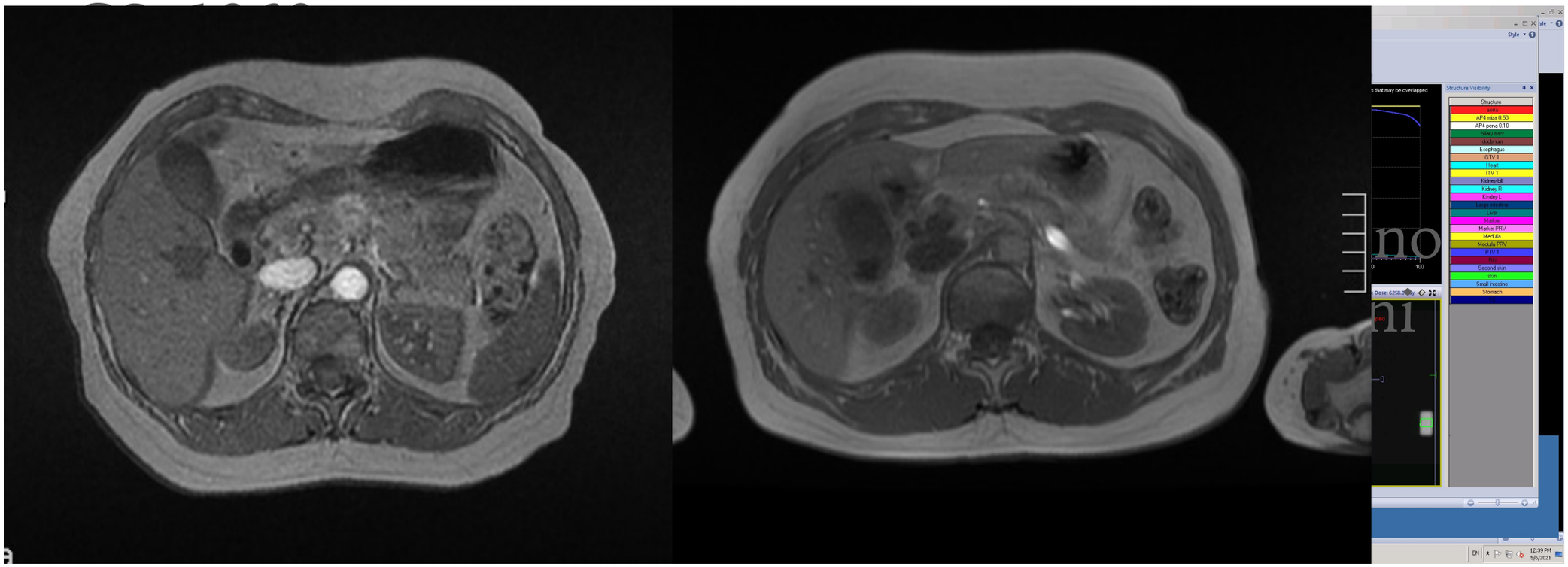






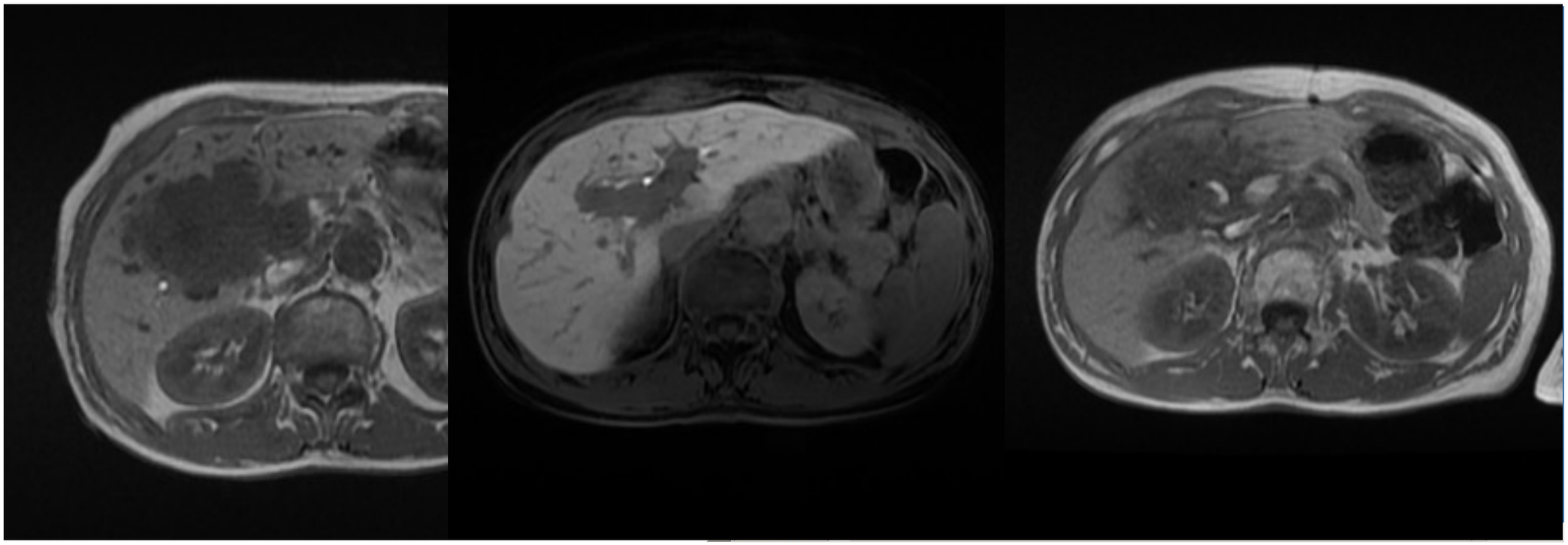
- Solitarni zasevek v možganih, premer 11,5 mm, inoperabilen
- 06/20 SRS 1 x 22,5 Gy
- 10/20 regres lezije z okolno levkoplakijo
- 02/21 radionekroza, brez ponovitve ali ostanka

PRIMER SBRT 1



- 02/20 novo nastal solitarni zasevek v jetrih, fokalna lezija velikosti 22 x 28 mm
- 06/20 vstavitev zlatih markerjev v jetra, SBRT 3 x 16 Gy, prehodna prekinitev Olapariba
- 09/20 CR, 02/21 CR

PRIMER SBRT 2



- 09/18 ponovitev bolezni (jetra 7,5 x 9 cm, bezgavki)
- KT II. reda, PR, vzdrževalno Olaparib
- progres lezije v jetrih
- 01/20 vstavitev zlatih markerjev v jetra, SBRT 5 x 8 Gy, prehodna prekinitev Olapariba
- 05/20 regres, 10/20 počasen progres, 01/21 KT III. reda

PRIHODNOST: PARP INHIBITORJI ALI IMUNOTERAPIJA IN SOČASNA RT

- Raziskave v teku

TABLE 3 | Select ongoing clinical trials of radiation combinations.

Description	Phase	Disease site	NCT number	Agent(s)	Sponsor
Poly(ADP-ribose) polymerase + radiation					
Olaparib and Radiotherapy in head and neck cancer	I	Squamous cell carcinoma of the larynx stage II–III	NCT02229656	Olaparib 25–300 mg BID	The Netherlands Cancer Institute
Phase I study of olaparib combined with cisplatin-based chemoradiotherapy to treat locally advanced head and neck cancer (ORCA-2)	I	High-risk locally advanced HNSCC	NCT02308072	Olaparib 50–200 mg BID Cisplatin 35 mg/m² Q week	Cancer Research UK
Olaparib and radiotherapy in inoperable breast cancer	I	Breast cancer or local recurrence of breast cancer, which is inoperable or/and metastatic, including inflammatory breast cancer	NCT02227082	Olaparib 25–400 mg BID	The Netherlands Cancer Institute
Veliparib with or without radiation therapy, carboplatin, and paclitaxel in patients with stage III non-small cell lung cancer that cannot be removed by surgery	I/II	Unresectable stage IIIA/IIIB, non-small cell lung cancer	NCT01386385	Arm I Carboplatin, Paclitaxel Arm II Carboplatin, Paclitaxel, Velaparib	NCI; Southwest Oncology Group
Veliparib and combination chemotherapy in treating patient with locally advanced rectal cancer	II	Locally advanced adenocarcinoma of the rectum, Stage II/III	NCT02921256	Arm I (mFOLFOX6, capecitabine) Arm II (mFOLFOX6, capecitabine, veliparib)	NCI; NRG Oncology
Immunotherapy + radiation					
FLT3 ligand immunotherapy and stereotactic radiotherapy for advanced non-small cell lung cancer	II	Stage III/IV non-small cell lung cancer not amenable to curative therapy	NCT02839265	FLT3 ligand therapy (CDX-301) with SBRT	Albert Einstein College of Medicine, Inc.
Checkpoint blockade immunotherapy combined with stereotactic body radiotherapy in advanced metastatic disease	II	Metastatic cancer with at least one lesion amenable to SBRT	NCT02843165	Checkpoint blockade immunotherapies (anti-CTLA-4 and anti-PD-1/PD-L1 antibodies) with SBRT	University of California, San Diego
ProstAtak® Immunotherapy with standard radiation therapy for localized prostate cancer	III	Localized prostate cancer meeting the NCCN criteria of intermediate risk or patients having only one NCCN high-risk feature	NCT01436968	Arm I ProstAtak®(AdV-tk) + valacyclovir Arm II Placebo + valacyclovir	Advantagene, Inc.
Ipilimumab and stereotactic body radiotherapy (SBRT) in advanced solid tumors	I/II	Metastatic cancer with at least one metastatic or primary lesion in the liver, lung, or adrenal gland	NCT02239900	Ipilumumab with SBRT	M.D. Anderson Cancer Center; Bristol-Myers Squibb
Pembrolizumab and chemoradiation treatment for advanced cervical cancer	II	Locally advanced cervical cancer stage IB1 with lymph nodes or IB2–IVA	NCT02635360	Arm I Cisplatin-based chemoradiation with consolidative pembrolizumab × 3 cycles Arm II Chemoradiation with concurrent Pembrolizumab × 3 cycles	University of Virginia; Merck Sharp & Dohme Corp

PRIHODNOST: WART

- Ponovno obsevanje celega trebuha, medenice: abdominalna kopel v sklopu adjuvantnega zdravljenja
- Z novimi tehnikami obsevanja, z nižjimi dozami na ledvice, jetra, kostni mozeg
- Študije faze I, II: sprejemljiva toksičnost? dobrobit adjuvantnega obsevanja?
- OVAR-IMRT-02, prospektivna študija faze II, Arians, 2019