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Radiotherapie van levermetastasen: exotische therapie of oprukkende mogelijkheid?

- 69ste Geneeskundige Dagen van Antwerpen
- Dr Reinhilde Weytjens

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Radiotherapie van levermetastasen:

- Klassieke RT: 2 Gy, 30-35 fracties.
- Stereotactic body RT (SBRT): 10-20 Gy, 1-5 fracties.
- Weefsels bestaan uit functionele subunits.
  - Functioneren onafhankelijk van elkaar (parallel)
  - Functioneren in coöperatie (serie)
  - Clonogene cellen: kunnen gedifferentieerde cellen, door radiotherapie beschadigd, vernieuwen.

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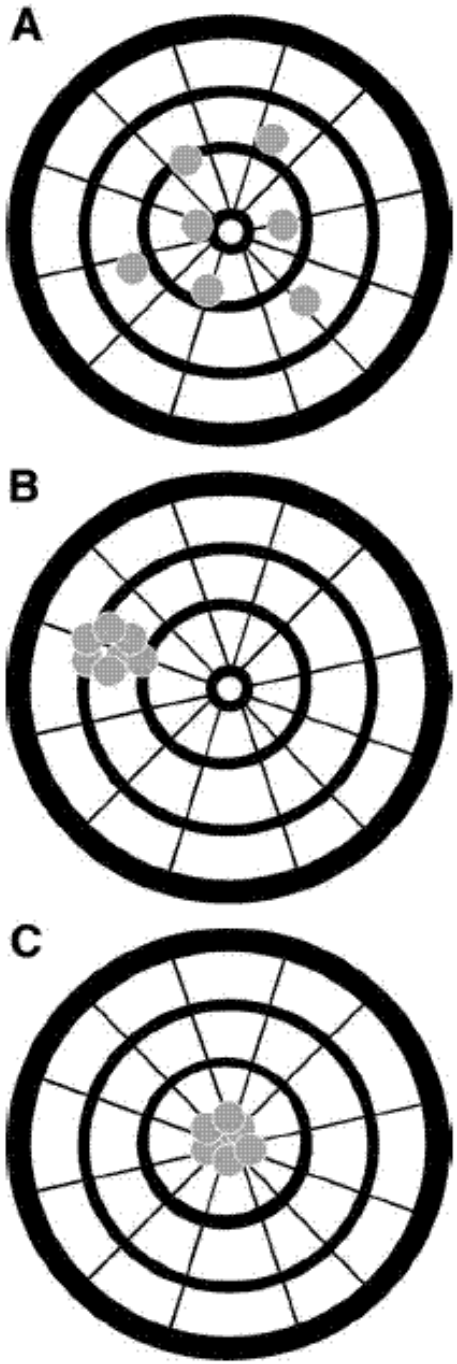
Radiotherapie van levermetastasen:

- Extracraniële radiochirurgie (1 fractie)
- Extracraniële stereotactische radio-ablatie
- Stereotactic Body Radiation Therapy SBRT
- Stereotactic Ablative Body Radiotherapy (SABR).



Accuraat maar niet precies

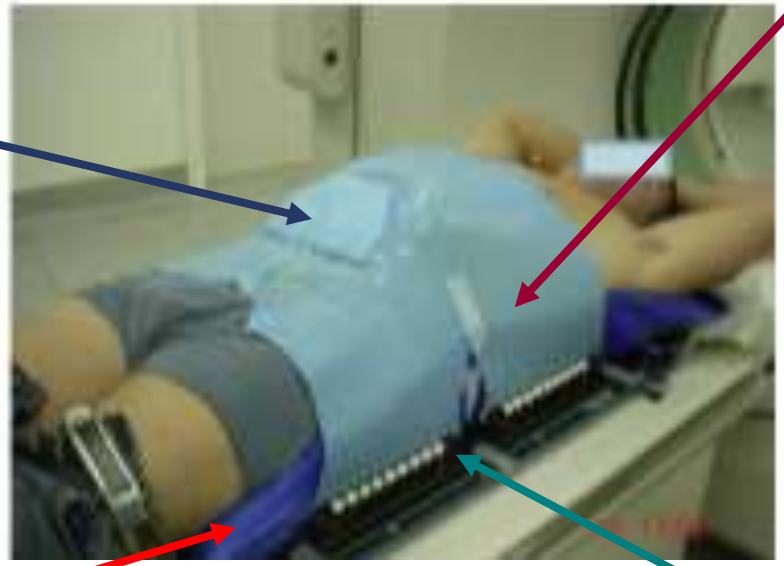
Precies maar niet accuraat

Accuraat en precies

- **Stereotactisch**: tumorpositie vs coördinaten systeem.
- **Body**: itt intracranieel

Thermoplastic
Immobilistie materiaal

Compressieblok
Uit Styrofoam



Vacuumkussen

Geïndexeerde Carbon
Fiber bak

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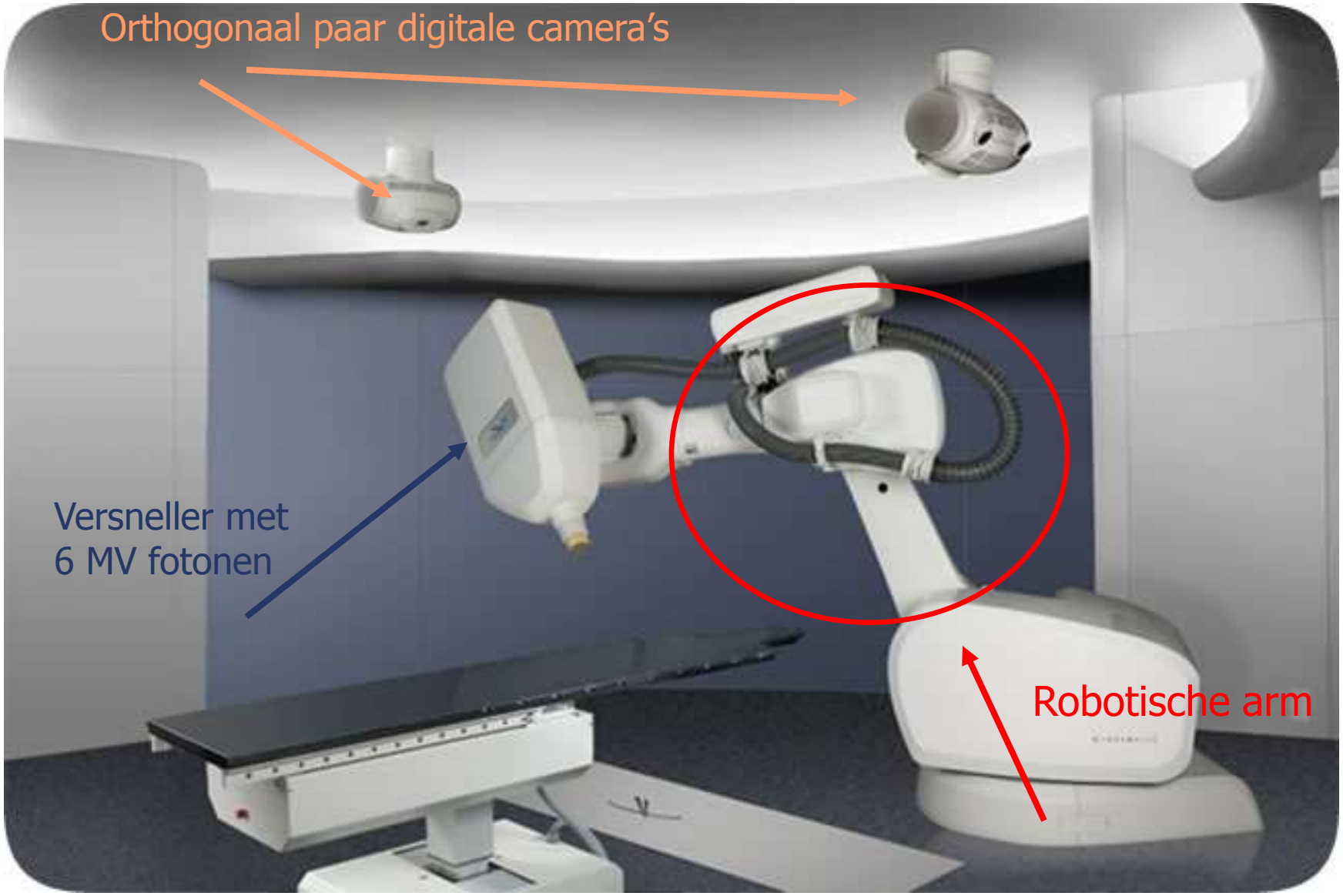
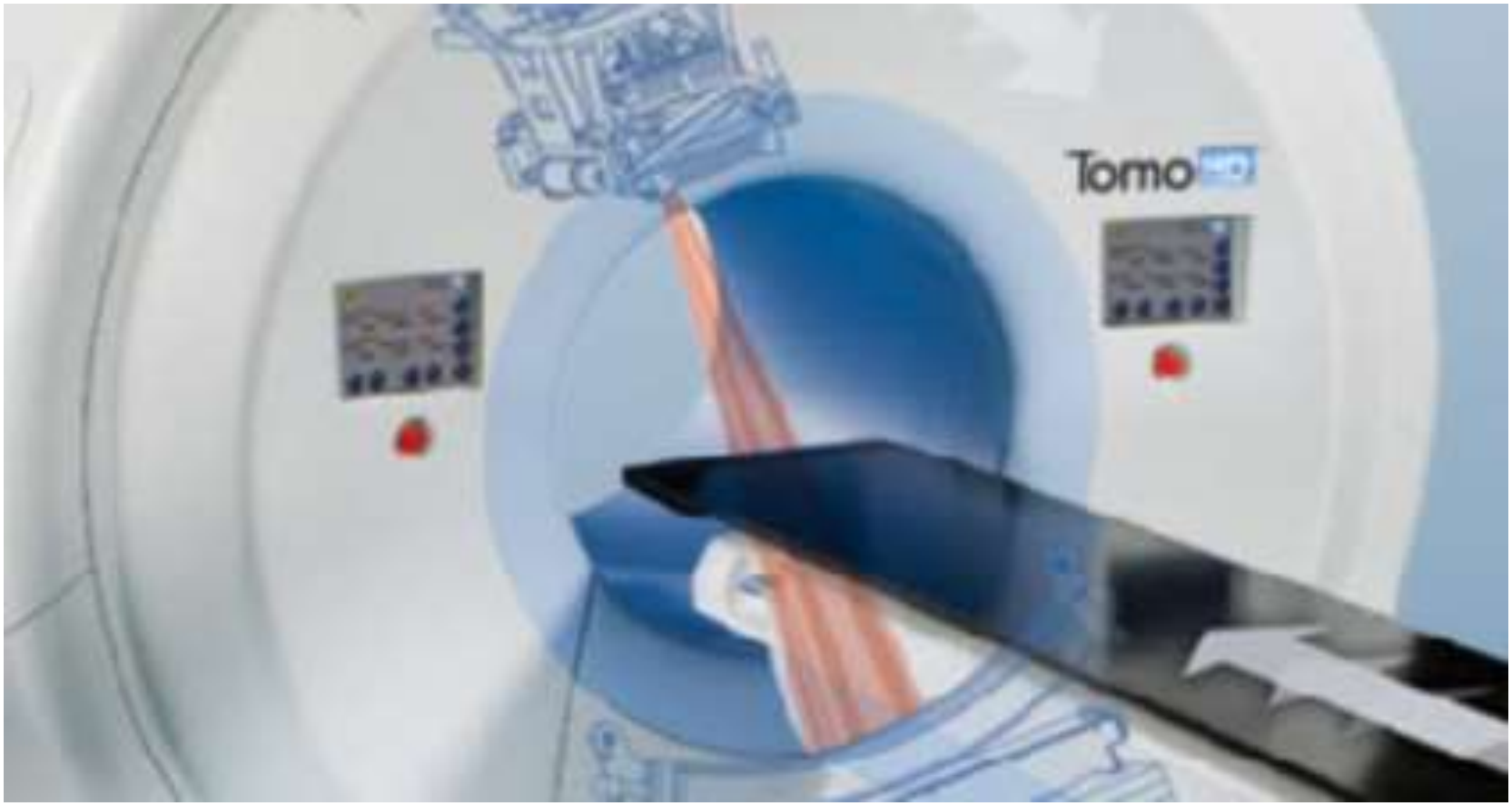
SBRT

- Comfortabele positionering
- Bewegingscontrole:
  - Beperken
    - Abdominale compressie
    - Adem inhouden
  - Gating
  - Tracking
- Patiëntenselectie


Orthogonaal paar digitale camera's
Versneller met
6 MV fotonen
Robotische arm

Beeldvorming met kV



CT scan + Bestraling.

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Radiotherapie van levermetastasen

- Technisch mogelijk
- Nuttig?
  - Bestaan oligometastasen?
  - Gepubliceerde resultaten
  - Gunstige tolerantie voor de patiënt
  - Combinatie met systemische therapie
  - Mogelijke nevenwerkingen

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Hypothese:

1. Niet alle metastasen zijn diffuus. Oligometastasen bestaan.
2. Agressieve locale therapie hiervoor kan leiden tot lange termijn ziektecontrole.

Evidenties voor deze hypothese:

- Heelkundige reeksen van oligometastasen van colon, sarcoma, melanoma, borst
- Fong et al, Scheele et al : 30-40 % 5 jaarsoverleving in ptn met resectie van levermetastasen (colorectaal)

Helaas zijn veel patiënten geen kandidaat (meer) voor heelkunde: anatomische localisatie, grootte, medische toestand, wens van de pt

Andere ablatieve technieken.

Combinaties

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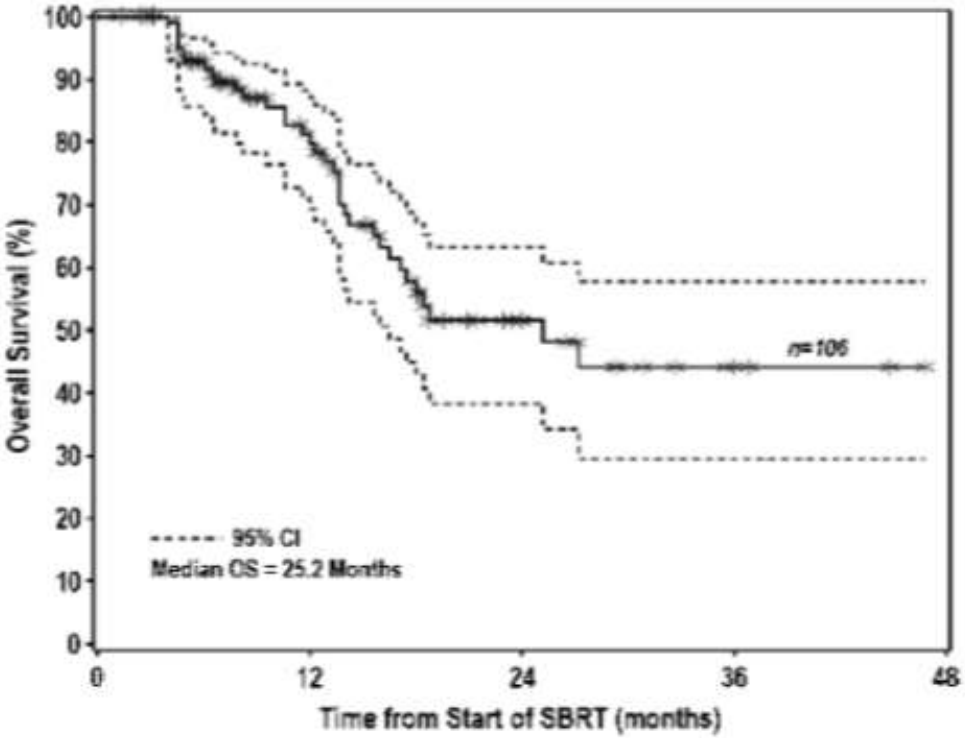
Liu et al. Translational Oncology (2013) 6, 442-446



- 62 ptn, 106 letsels
- 3-5 fracties
- 50-60 Gy
- 4 jaarsoverleving vergelijkbaar HK

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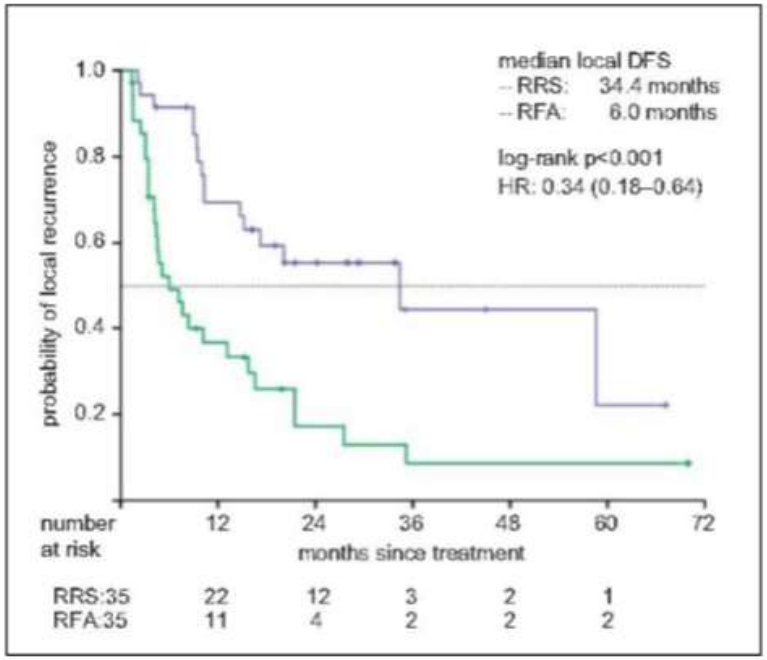
Percutane RFA vs Robotic Radiosurgery for salvage treatment of colorectal liver metatases. Stingzing et al,

Acta Oncologica (2013) 52: 971-977



- 30 pts, 35 letsels, match volgens aantal en diameter van de letsels in een RFA cohort.
- Significant langere DFS met RRS (34,4 vs 6 m)
- Geen verschil andere eindpunten

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Mogelijke nevenwerkingen

- Radiation Induce Liver Disease (RILD)
- Intestinale ulceraties
- Mogelijke interactie met VEGF inhibitors

- Positionering
- Ademhaling
- Radio opake markerplaatsing

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Observaties darmtox bij SBRT prostaatca

Table 4. Comparison of late urinary and late rectal toxicity from EPIC between consecutive daily treatments (QD) and those delivered every other day (QOD)

	QD	QOD	*p* value*
Urinary			
Overall urinary QOL score 4–6 ("mostly dissatisfied" or "unhappy" or "terrible")	19% (4/21)	5% (1/20)	0.34
Baseline urinary QOL score 3 ("mixed")	38% (8/21)	15% (3/20)	0.16
Rectal			
Any item† score 4–5 ("moderate" or "big problem")	38% (8/21)	0% (0/20)	0.0035
Overall rectal QOL‡ score 4–5 ("moderate" or "big problem")	24% (5/21)	0% (0/20)	0.048
Baseline rectal QOL score 2 ("very small problem")	19% (4/21)	0% (0/20)	0.11

Behandeling om de andere dag ipv alle dagen

King et al, IJROBP 2008

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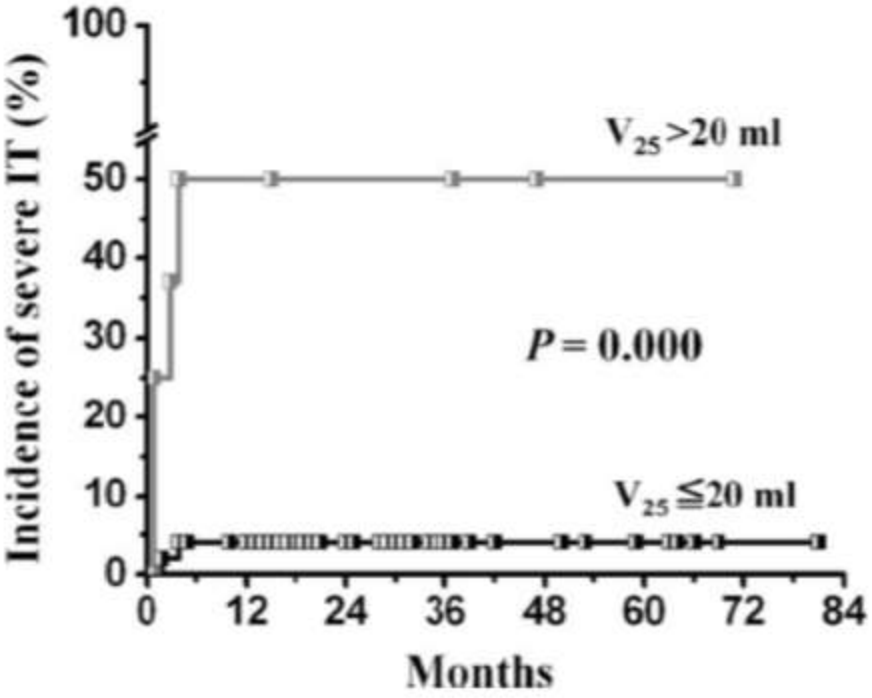
Severe intestinal toxicity after stereotactic ablative radiotherapy for abdominopelvic malignancies.

Int J Colorectal Dis. 2013: 1707-1713

202 ptn
3 fracties
Predictief voor zware intestinale toxiciteit:

- V25 > 20 cc
- R/ duur 3 dd vs 4-8 dd



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Barney et al. Increased bowel toxicity in patients treated with VEGF Inhibitor after SBRT. IJROBP 2013; 87(1): 73-80

Characteristic	All patients (N = 76)	Patients with no SBI (n = 69)	Patients with SBI (n = 7)	*P* value
Pre-SBRT SBI risk factors [n (%)]				
Previous RT	11 (15)	10 (15)	1 (14)	>.99
Previous bowel resection	31 (41)	28 (41)	3 (43)	>.99
SBRT				
Time from cancer diagnosis to SBRT (mo)				.75
Median	34	33	36	
Range	1-158	1-158	14-83	
SBRT prescription dose (Gy)				.76
Median	50	50	[illegible]	
Mean	48.9	48.7	[illegible]	
Range	28-60	28-60	[illegible]	
Fractions [n (%)]				
1	3 (4)	3 (4)	[illegible]	
3	24 (32)	21 (30)	[illegible]	
5	49 (65)	45 (65)	[illegible]	
Maximum bowel dose (Gy)				
Median	31.6	31.3	[illegible]	
Range	7.2-55.3	7.2-55.3	[illegible]	
Systemic therapy				
Systemic regimens before SBRT (n)				
Median	1	1	1	
Range	0-4	0-4	0-4	
Systemic regimens after SBRT (n)				.02*
Median	1	0	2	
Range	0-5	0-5	1-2	
Systemic agent category [n (%)]				
Alkylator	37 (49)	32 (46)	5 (71)	.26
Antimetabolite	33 (43)	31 (45)	2 (29)	.69
VEGFI	30 (40)	23 (33)	7 (100)	.0009*
Antibody type (bevacizumab)	23 (30)	17 (25)	6 (86)	.0026*
TKI (sorafenib, pazopanib, sunitinib)	9 (12)	7 (10)	2 (29)	.19
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Topoisomerase inhibitor	9 (12)	7 (10)	2 (29)	.19
Immune modulator	9 (12)	8 (12)	1 (14)	>.99

Abbreviations: RT = radiation therapy; SBI = serious bowel injury; SBRT = stereotactic body radiation therapy; TKI = tyrosine kinase inhibitor; VEGFI = vascular endothelial growth factor inhibitor.
* Statistically significant

38 % zware darmtoxiciteit in de groep v 26 ptn die VEGFI kregen binnen de 6 maanden na SBRT

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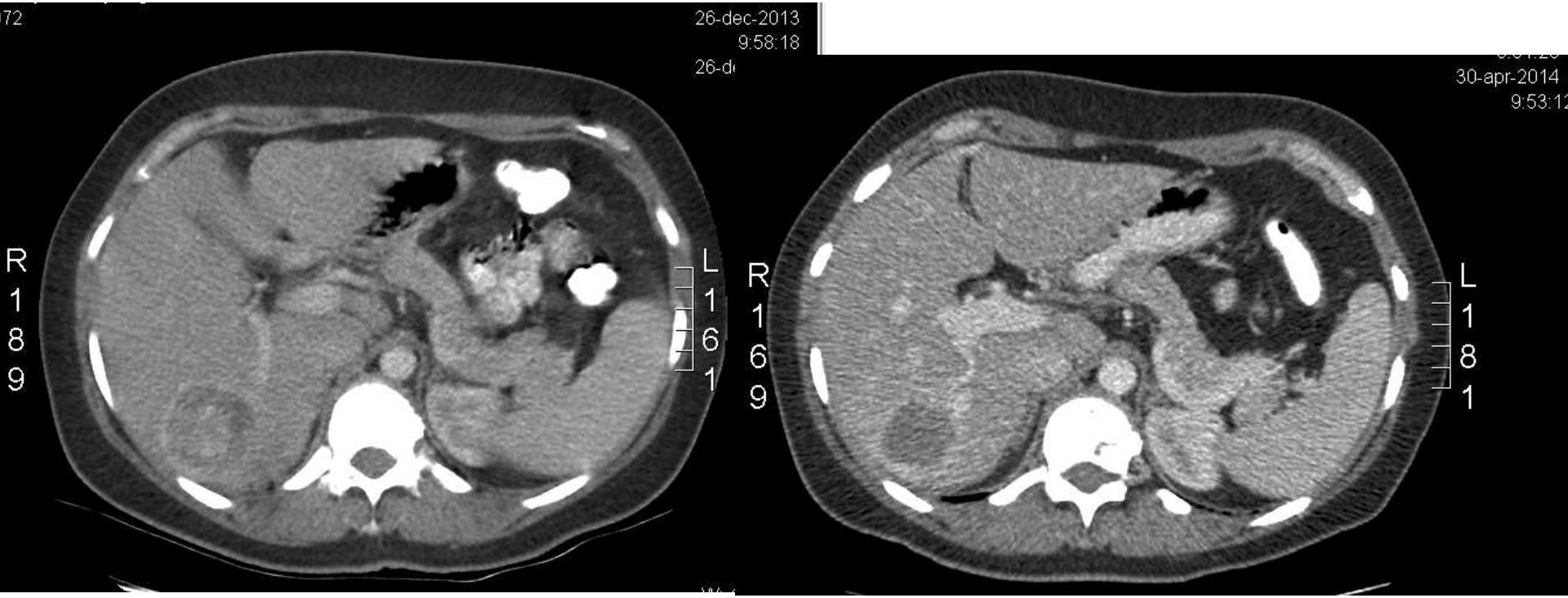
Radiotherapie van levermetastasen

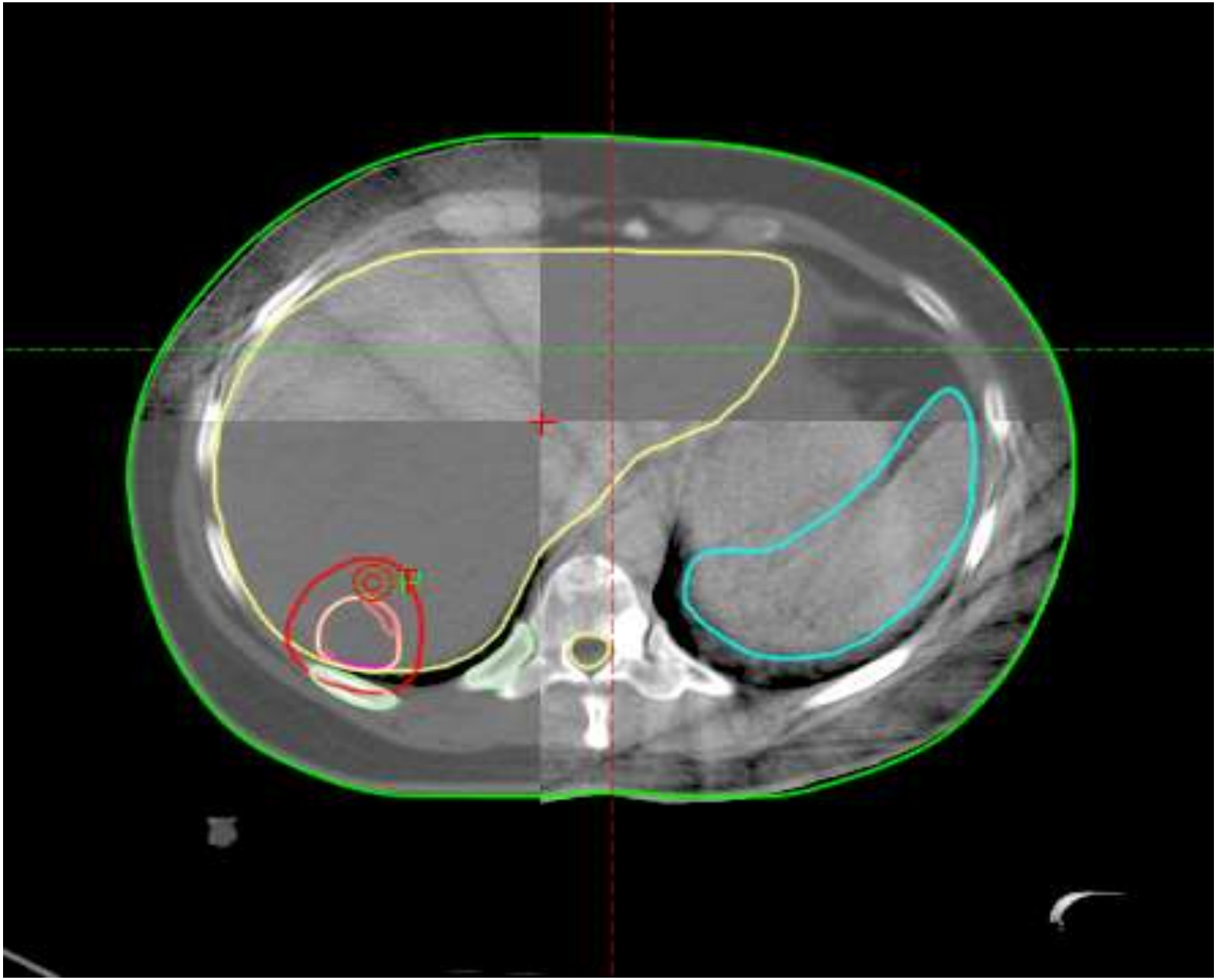


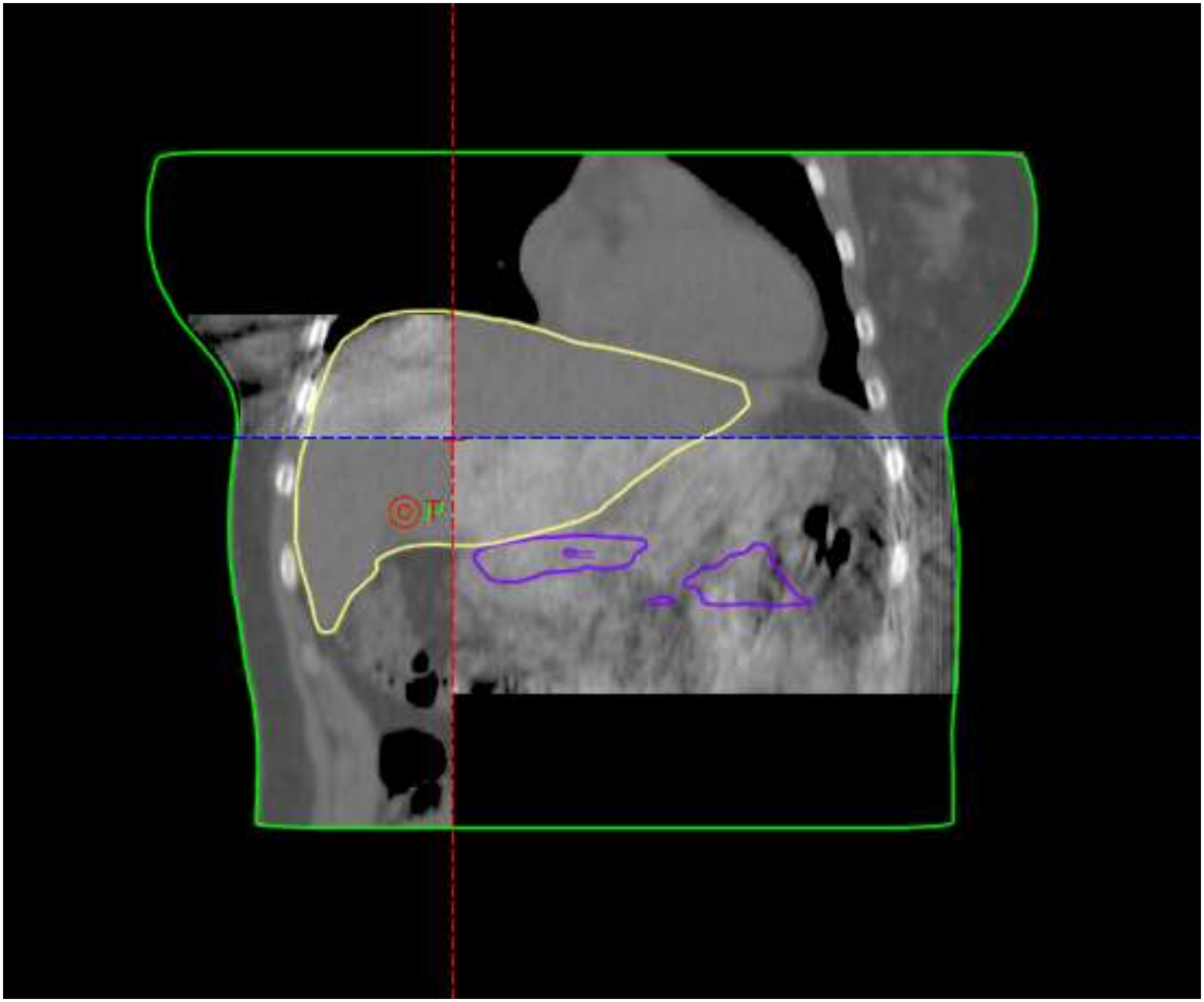
Dec 2013: Progressieve ziekte: levermetastase.
MOC: hoge dosis radiotherapie

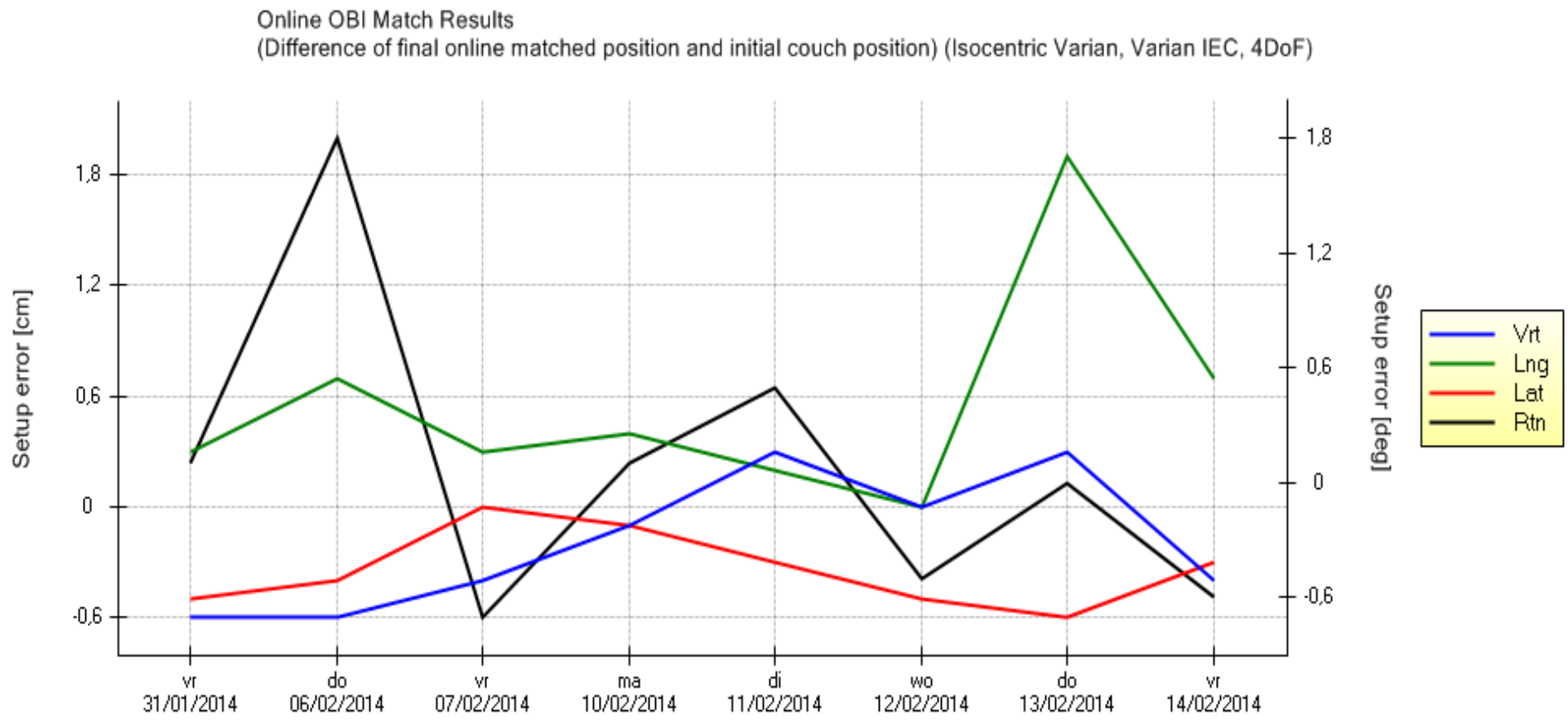
- 12/2013: beslissing RT
- 01/2014: RT
- 02/2014: CT grafische stabiel
- 04/2014: regressie
- Geen wijziging in systemische therapie
- Gunstige tolerantie

21/05/2014 08:54	30/04/2014 08:45	10/04/2014 09:48	20/03/2014 10:52	27/02/2014 08:35	06/02/2014 10:05	16/01/2014 10:11	26/12/2013 08:48	05/12/2013 10:00
33	33	34	+ 35	+ 49	+ 58	+ 50	+ 39	33

H
103.9 %
norm







Object Type: CBCT Plan: 1LEVER4 Chart Type: Online OBI Match Results

Radiotherapie levermetastasen

- “superpalliatief “schema:
  - Ptn met pijn -> cortico nood /leverkapselpijn.
  - Mechanische hinder -> zitten wordt moeilijk

- Borgelt et al, IJROBP 1981; 7: 587-591:
  - 7 x 3 Gy: 55 % respons op de pijn.
  - Gelijkaardige schemata (korter) bleken even goed.

- Volledige of halve leverbestraling met zeer eenvoudige opstelling.

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2013:
In kader van RIZIV project:
“Innovatieve radiotherapie technieken”:

- Nationale guidelines
- Registratie van (oa) SBRT levermetastasen.

Module SBRT – Standard indication

Centre RT	Enregistrements depuis 1/08/2013	Primary lung	Hepatic metastases	Primary spinal lesion	Spinal metastases	Lung metastases
1	15	13				2
2	16	15				1
3	10	8				2
4	51	19	10			22
5	37	29	2			6
6	5	5				
7	31	26	1			4
8	33	20	1		5	7
9	14	7				7
10	26	14	3		5	4
11	94	56	10	3	8	17
12	31	26				5
13	38	18	3			17
Total	**401**	**256**	**30**	**3**	**18**	**94**

Module SBRT – Standard indication

Indications

SBRT is recommended for patients with oligo liver metastases. It is most often proposed for inoperable lesions:

- Inoperability because of because of the lesion location
- Inoperability because of risks of general anesthesia in a elderly, pretreated patient cohort
- Inoperability because of other surgical consideration
- Inoperability because of patient refusal

It is however possible to propose the less invasive SBRT treatment to operable patients too, because 3y control rates are comparable to surgical results (table 1).

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Dank voor uw aandacht

Vragen?