

**From better technology to better clinical outcome:**

**Clinical implementation of SRS/SBRT/SABR with RapidArc and FFF beams (on TrueBeam)**

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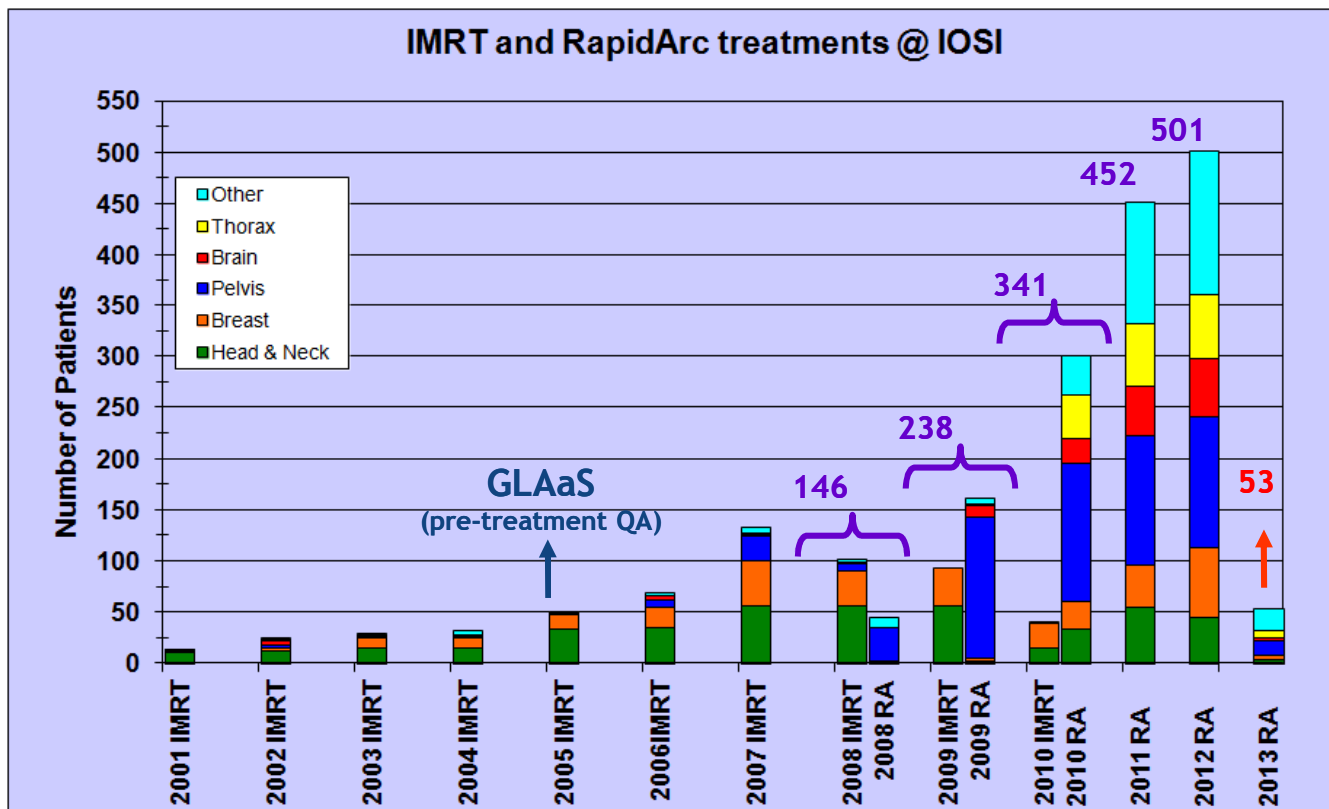
Scientific Advisor, Humanitas Institute, Milan-Rozzano, Italy

Scientific Advisor, Varian Medical Systems, Switzerland

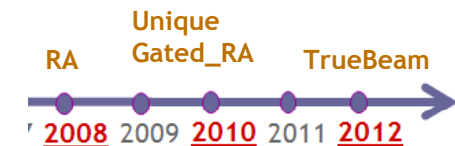
# The power of RapidArc: IOSI

First RapidArc treatment @ IOSI: Sept 8<sup>th</sup>, 2008

As per today: 1474 RapidArc patients treated at IOSI (1860 plans)



Migration of the IMRT programme to RapidArc in 2010



Statistics for

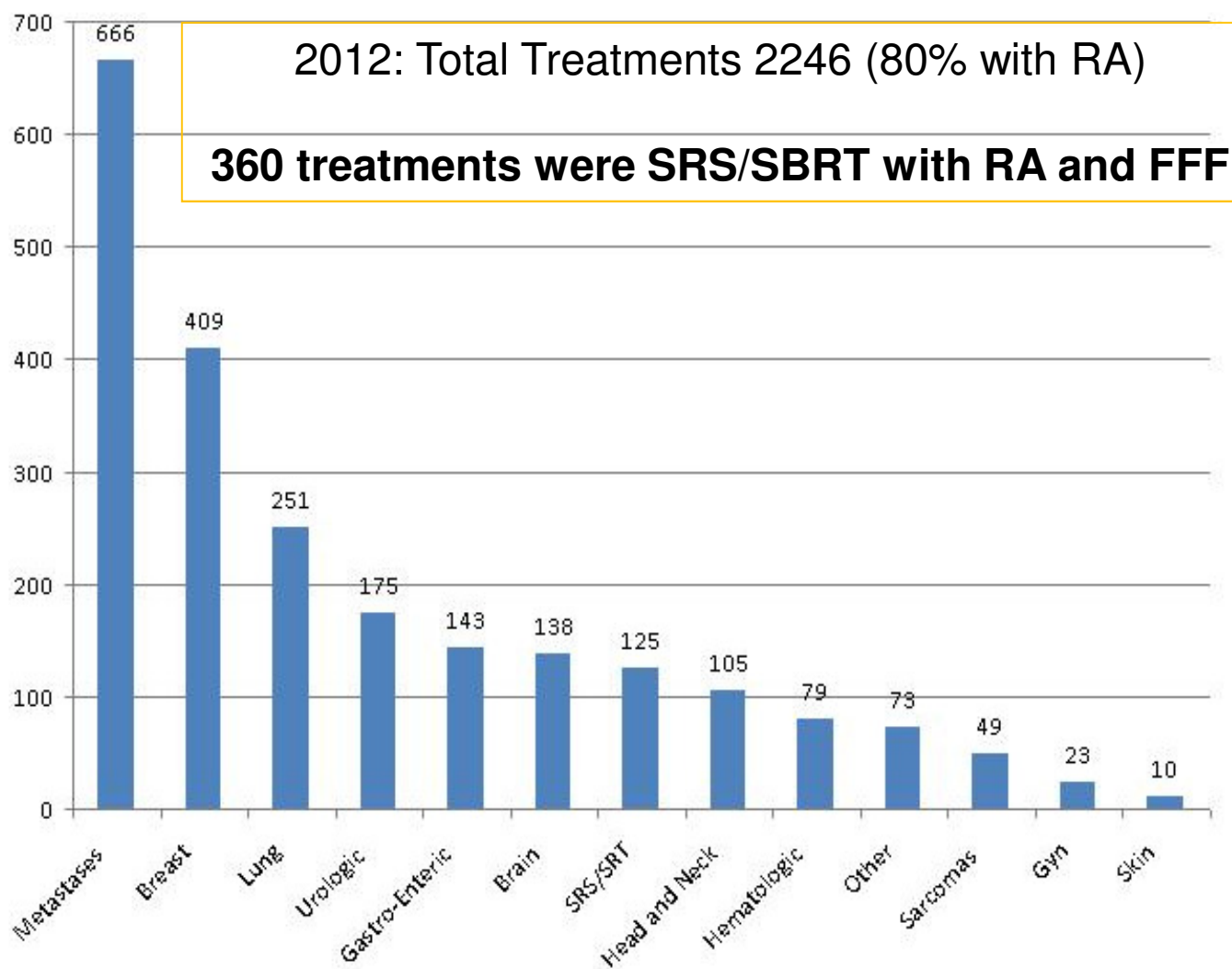
2009 - 2010 - 2011 - 2012:

# pat RA/total = 25% - 50% - 79% - 77%

Statistics for 2013

# pat RA/total = 78.5%

# The power of RapidArc: Humanitas

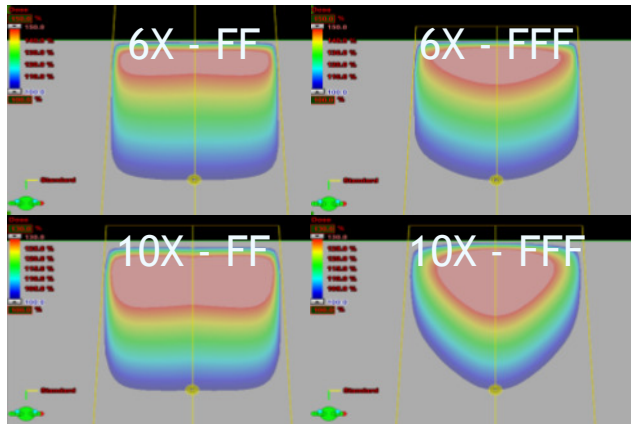


# What TrueBeam brought into the clinics

- **New beam delivery: high intensity mode or FFF mode**
- Advanced VMAT-RapidArc capability
- New imaging modalities (e.g. imaging during delivery)
- New technology and control systems: improved accuracy
- Ready for motion management and tracking
- Upcoming further technology (e.g. 6DoF couch)



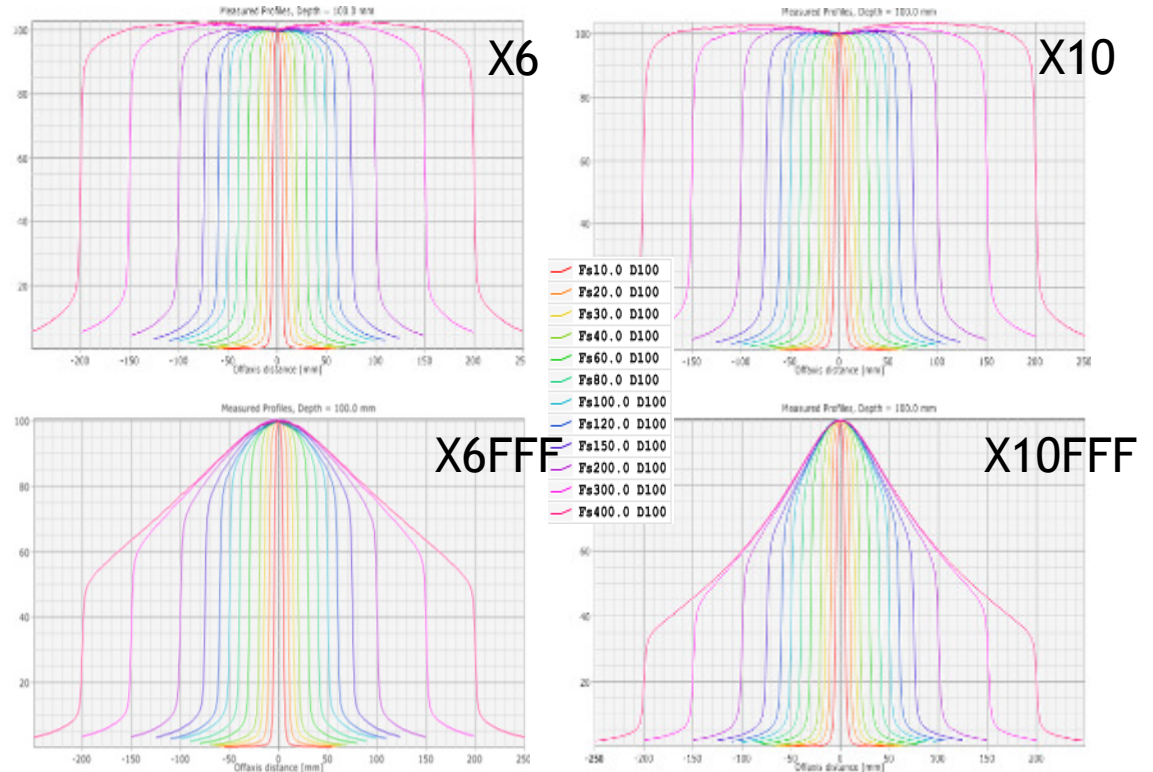
# TrueBeam: FFF versus FF: Profiles



Non-flatness increases with energy  
 Up to 3x3 cm<sup>2</sup>, difference in the profile for flattened and FFF is neglectable

Sharper penumbra in shallow depths for lower energies (shorter reach of secondary electrons)

Faster diverging penumbra with depth for lower energies (more likelihood of lateral scattering)



# Why FFF ?

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- unflattened beams *can* be used for IMRT and SBRT
- *increased dose rate* – reduction of delivery time *Fu et al, PMB (2004)*
- SBRT – high fractional doses (DIBH, gating)
- reduced scatter, leaf transmission and radiation head leakage *Kragl et al, R&O (2009)*
- reduced variation of beam quality across the beam *Georg et al, MP (2010)*
- *reduced peripheral exposure* *Kry et al, PMB (2010)*
- compared to conventional RT, IMRT has been found to increase PD *Kry et al, PMB (2010)*

# TRUE BEAM initial clinical experience with FFF beam

70 FFF treatments analyzed



52 SBRT for lung lesions:  
•Doses: 48 Gy in 4 fract.  
•Toxicity: 2 case of G2 and 3 G3 esophagitis



12 SBRT liver lesions:  
•Doses: 75 Gy in 3 fract.  
•Toxicity: 2 case of G2 nausea/vomit

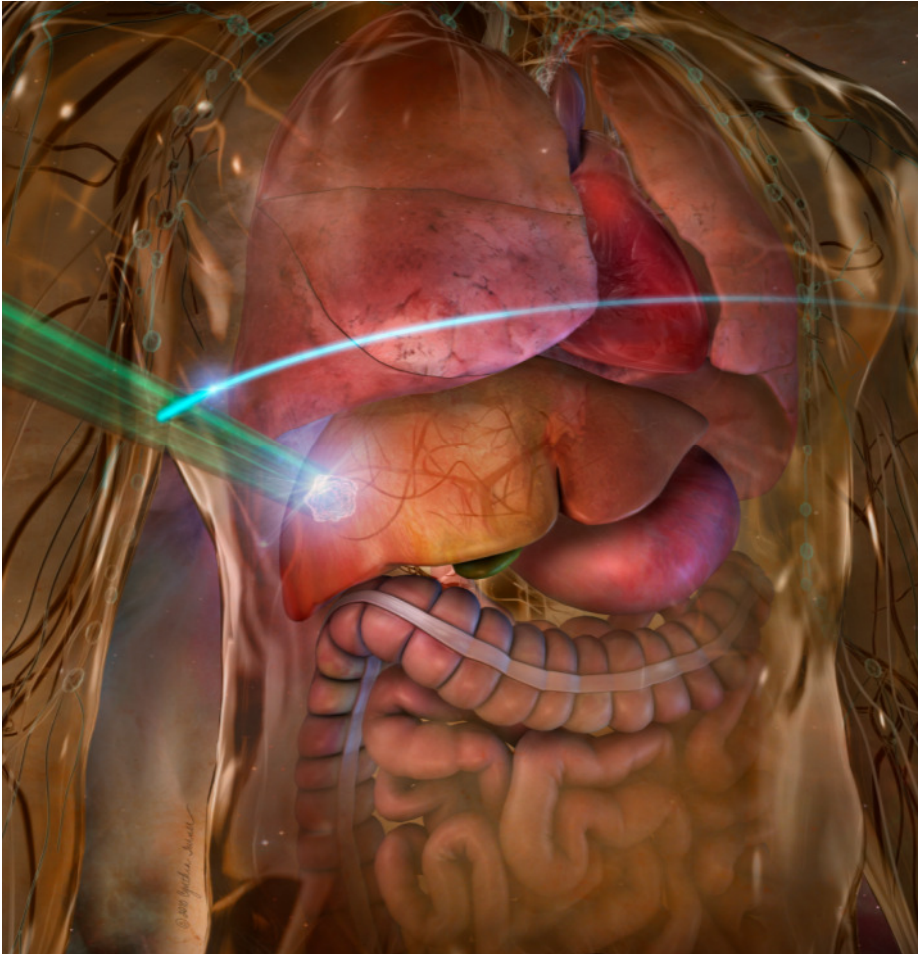


6 SBRT for abdominal nodes:  
•Doses: 45 Gy in 6 fract.  
•Toxicity: none

In 55/70 pts, early clinical outcome was assessable (very shor FU):  
•10 complete response,  
•26 partial response,  
•13 stable disease.  
•6 local progression.  
**90% of Local Control achieved in irradiated lesions**

# RapidArc (on TB) clinical results

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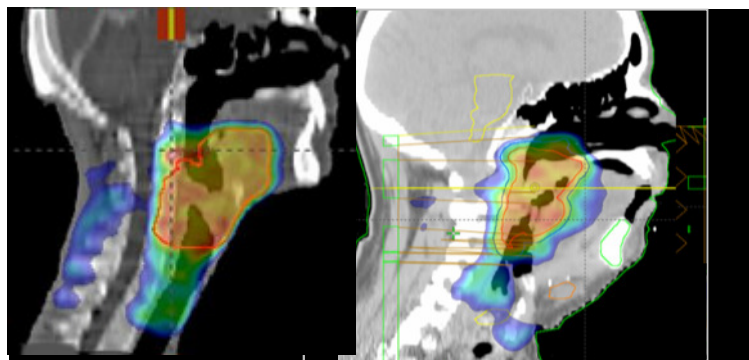
- Head and Neck
- Lung
- Prostate
- Liver
- Pancreas

**Focus on SRS and SABR**



# Does RapidArc have a role in Head and Neck?

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2009 Vanetti E et al oro pharynx, hypo pharynx and larynx. Radiother. Oncol.

2009 Verbakel W et al. head and neck cancer. Int. J. Radiat. Oncol. Biol. Phys.

2010 Doonaert P et al locally advanced head and neck cancer. Int. J. Radiat. Oncol. Biol. Phys.

2010 Scorsetti M et al. Early clinical experience in head and neck cancer patients. Radiat. Oncol.

2010 Jacob V et al head an neck tumors. Strahl. Onkol.

2011 Doonaert et al. Subm. Gland sparing with RA. Radiat. Oncol.

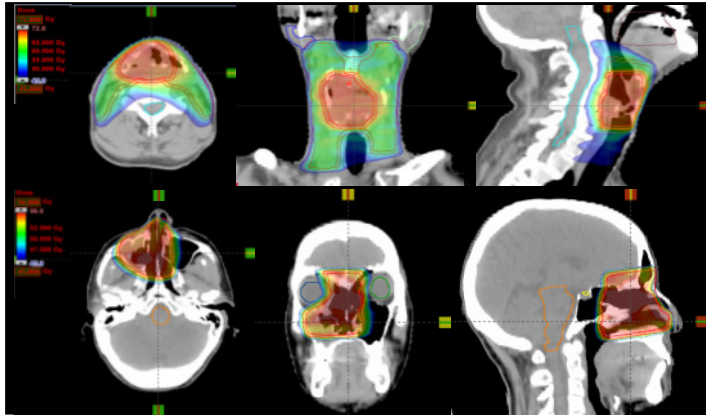
2011 Wiezorek et al. RA, IMRT and tomotherapy. A comparison. Radiat. Oncol.

2011 wiehle et al. RA vs IMRT in HN a comparison. Strahl. Onkol.

2012 Kahn et al. RA and IMRT with Acuros. IJROBP

2012 Alongi et al. Phase II trial: SIB with RA + cetuximab Strahl. Onkol.

# Head and Neck: Clinical results at Humanitas Institute



To date: >300 patients treated

Standard prescription:

Radical: 33 fractions, 69.96 Gy on T&N+ , 54.45 Gy on prophylactic nodes

Adjuvant: 30 fractions, 66 Gy on T&N

Toxicity report on first 45 patients:

|                   |                   |    |
|-------------------|-------------------|----|
| Site              | Oral Cavity       | 7  |
|                   | Nasopharynx       | 3  |
|                   | Oropharynx        | 16 |
|                   | Hypopharynx       | 1  |
|                   | Larynx            | 10 |
|                   | Paranasal Sinuses | 6  |
|                   | Other             | 2  |
| Dose Prescription | Group A:          |    |
|                   | 69.96/54.45Gy     |    |

|                  |             | All | No ch | CDDP | Cetuximab |
|------------------|-------------|-----|-------|------|-----------|
| Completion of RT | Completed   | 43  | 10    | 16   | 17        |
|                  | Interrupted | 2   | 0     | 0    | 2         |
| Mucositis        | G0          | 1   | 0     | 1    | 0         |
|                  | G1          | 15  | 3     | 7    | 5         |
|                  | G2          | 8   | 1     | 4    | 3         |
|                  | G3          | 12  | 1     | 2    | 9         |
| Dermatitis       | G0          | 1   | 1     | 0    | 0         |
|                  | G1          | 18  | 3     | 11   | 4         |
|                  | G2          | 11  | 1     | 3    | 7         |
|                  | G3          | 6   | 0     | 0    | 6         |

# Head and Neck: RA in elderly

## Prospective phase II trial of cetuximab plus VMAT-SIB in locally advanced head and neck squamous cell carcinoma

**Tab. 2 Description of the population of study with patients stratified for T and N stage**

| Number of patients, <i>n</i><br>Percent of patients, % | <i>n</i> | Clinical T stage |    | Total |
|--|----------|------------------|----|-------|
|  |          | T3               | T4 |       |
| <b>Clinical N stage</b>                                |          |                  |    |       |
| NX   | <i>n</i> | 1                | 0  | 1     |
|  | %        | 4                | 0  | 4     |
| N0   | <i>n</i> | 2                | 0  | 2     |
|  | %        | 9                | 0  | 9     |
| N1   | <i>n</i> | 2                | 4  | 6     |
|  | %        | 9                | 18 | 27    |
| N2   | <i>n</i> | 4                | 8  | 12    |
|  | %        | 18               | 36 | 54    |
| a  | <i>n</i> | 1                | 1  | 2     |
|  | %        | 4                | 5  | 9     |
| b  | <i>n</i> | 2                | 5  | 7     |
|  | %        | 9                | 23 | 32    |
| c  | <i>n</i> | 1                | 2  | 3     |
|  | %        | 5                | 9  | 14    |
| N3   | <i>n</i> | 0                | 1  | 1     |
|  | %        | 0                | 5  | 5     |
| <b>Total</b>   | <i>n</i> | 9                | 13 | 22    |
|  | %        | 41               | 59 | 100.0 |

Toxicity evaluation and follow up

**Tab. 3 Description of the recorded toxicities stratified for type and grading (G)**

|                             | <i>n</i> | %    |
|-----------------------------|----------|------|
| <b>Hematologic toxicity</b> |          |      |
| Yes                         | 4        | 18   |
| Anemia G1                   | 3        | 14   |
| Platelet loss G2            | 1        | 4    |
| No                          | 18       |      |
| <b>Skin toxicity</b>        |          |      |
| Yes                         | 20       | 90.0 |
| G1                          | 4        | 18   |
| G2                          | 8        | 36   |
| G3                          | 8        | 36   |
| No                          | 2        | 10   |
| <b>Mucosa</b>               |          |      |
| Yes                         | 20       | 9    |
| G1                          | 2        | 9    |
| G2                          | 8        | 36   |
| G3                          | 10       | 45   |
| No                          | 2        | 10   |
| <b>Dysphagia</b>            |          |      |
| Yes                         | 17       | 77   |
| G1                          | 12       | 54   |
| G2                          | 2        | 9    |
| G3                          | 3        | 14   |
| No                          | 5        | 23   |

**Tab. 1 Contraindications for radiochemotherapy**

|  |
|--|
| <b>Elderly</b><br>Age ≥ 70 years old   |
| <b>Unfit for limiting performance status</b><br>Performance status ≥ 2 according to ECOG or Karnovsky Performance Scale ≤ 60       |
| <b>Unfit for limiting comorbidities</b><br>Functional marrow, liver, and kidney activity limiting for the prescribing of cisplatin |

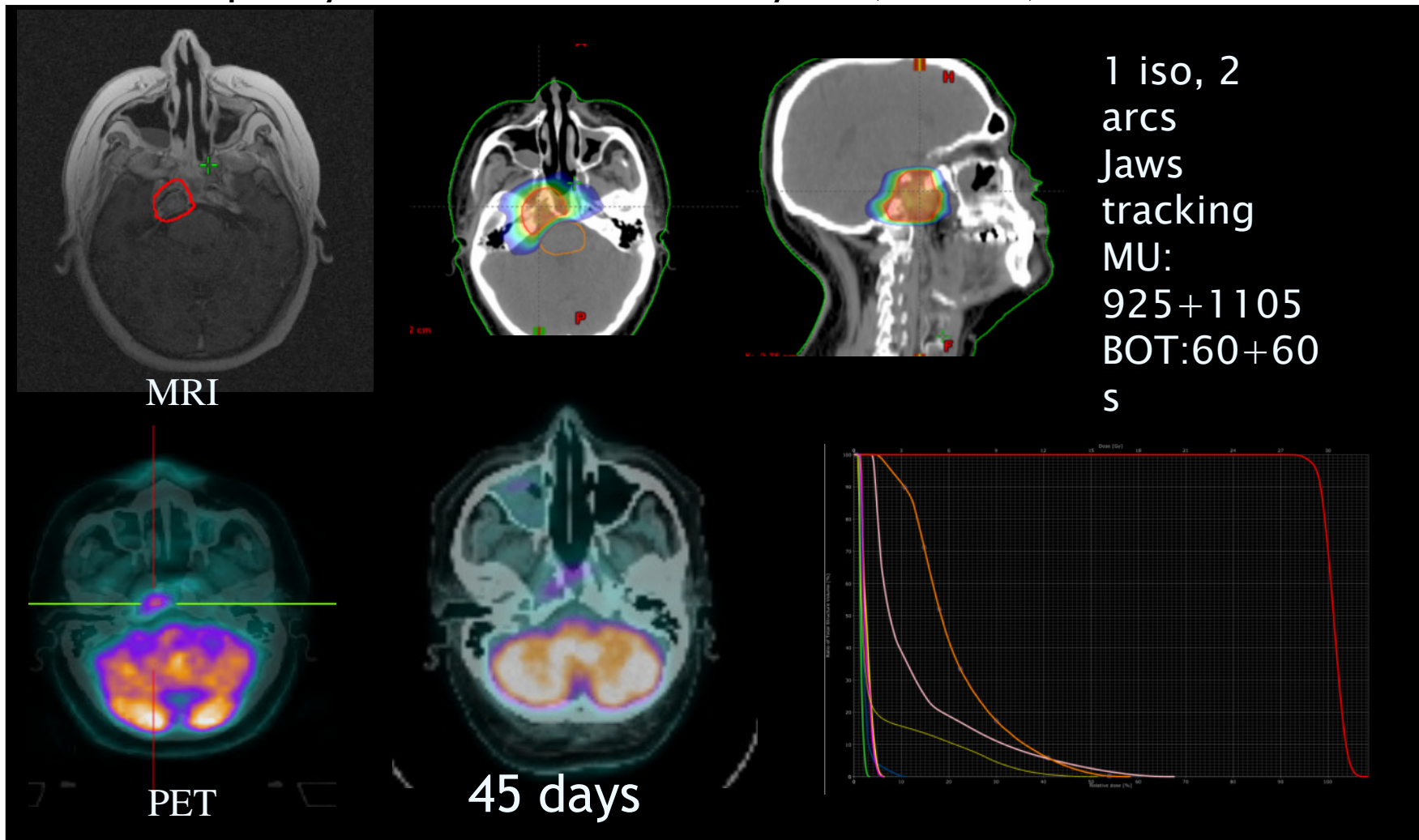
33 fractions: 1.65 and 2.12 Gy per fraction

### Conclusion

The toxicity data reported here are promising and encouraging in relation to the adoption of moderate hypofractionation with VMAT-SIB techniques. Longer follow-up is necessary to evaluate late toxicities, and definitive outcomes in terms of disease-free and overall survival.

# Head and Neck: what next? TrueBeam and FFF!

Nasopharynx re-treatment: 6Gy x 5; 10FFF; DR 2400.



# Does RapidArc play a role in Lung cancer?

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Verbakel et al. Radiother. Oncol. 2009

Ong et al. Radiother Oncol 2010;97:431

Scorsetti et al. Radiat. Oncol. 2010

Ong et al. Radiother. Oncol. 2010;97:437

Ong et al. IJROBP 2011

Palma et al. IJROBP 2011;79

Palma et al. IJROBP 2011;81

Chan et al. Radiother. Oncol. 2011

Kimura et al. IJROBP 2011

Trakul et al. IJROBP 2012

Bree et al. Med. Dosim. 2012

Seppala et al. Radiat. Oncol. 2012

Dehale et al. Radiother. Oncol. 2012

Verbakel et al. IJROBP 2012

# SBRT/SABR in early stage lung tumors

## Meta-analysis [Grutters JPC 2009]

|                        | CRT                   | SBRT                  | Protons               |
|------------------------|-----------------------|-----------------------|-----------------------|
| 2-year OS*<br>(95% CI) | <b>53%</b><br>(46-60) | <b>70%</b><br>(63-77) | <b>61%</b><br>(47-75) |
| 5-year OS*<br>(95% CI) | <b>19%</b><br>(15-24) | <b>42%</b><br>(34-50) | <b>40%</b><br>(24-55) |

*\*OS: overall survival corrected for % of medically inoperable patients*

CRT = conventional RT

SBRT = stereotactic body RT

# Stereotactic ablative radiotherapy (SABR)



Systematic review

Systemic review of the patterns of failure following stereotactic body radiation therapy in early-stage non-small-cell lung cancer: Clinical implications

Alexander Chi <sup>a,\*</sup>, Zhongxing Liao <sup>b</sup>, Nam P. Nguyen <sup>a</sup>, Jiahong Xu <sup>c</sup>, Baldassarre Stea <sup>a</sup>, Ritsuko Komaki <sup>b</sup>

**Table 2**

Reported survival outcome and local control in **35 studies**; SD = standard deviation.

|                                    | # Studies with available data | Mean ± SD     | Median (range)       |
|------------------------------------|-------------------------------|---------------|----------------------|
| <i>Overall survival (%)</i>        |                               |               |                      |
| 12 months                          | 15                            | 82.82 ± 11.43 | 83.00 (52.00–100.00) |
| 24 months                          | 21                            | 64.59 ± 15.49 | 65.40 (32.00–91.00)  |
| 36 months                          | 18                            | 57.67 ± 15.97 | 55.90 (32.00–91.00)  |
| 60 months                          | 9                             | 45.29 ± 20.10 | 47.00 (18.00–77.50)  |
| <i>Cause-specific survival (%)</i> |                               |               |                      |
| 12 months                          | 7                             | 93.67 ± 2.71  | 94.00 (88.00–96.00)  |
| 24 months                          | 15                            | 77.31 ± 9.93  | 82.00 (53.50–88.00)  |
| 36 months                          | 14                            | 72.01 ± 11.96 | 70.00 (53.00–90.50)  |
| 60 months                          | 7                             | 56.89 ± 16.27 | 50.00 (40.00–78.00)  |
| <i>Local control (%)</i>           |                               |               |                      |
| 12 months                          | 8                             | 91.81 ± 3.53  | 92.00 (85.30–96.00)  |
| 24 months                          | 11                            | 86.90 ± 9.68  | 88.00 (67.90–96.00)  |
| 36 months                          | 11                            | 80.62 ± 13.57 | 84.00 (57.00–95.00)  |
| 48 months                          | 1                             | 89.00 ± 0.00  | 89.00 (n/a)          |
| 60 months                          | 1                             | 86.00 ± 0.00  | 86.00 (n/a)          |

**Local control rates ≥90%**

[Chi A, 2010]

**Serious toxicity uncommon**

[Chi A, 2010]

**Quality of life maintained**

[van der Voort van Zyp N; Senan S, 2010]

**Limited decline in pulmonary function**

[Henderson M, 2008; Stephans KL, 2009; Phernambucq E, 2011]

# SBRT: RA with FFF modality

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What RA brings:

- Dose conformity to the tumor
- Sparing of healthy tissue

What Flattening Filter-Free Beams (FFF) brings:

- Reduction peripheral dose
- Higher dose rate
- Much higher dose per pulse
- Significantly faster RT

***IMPROVING TIME EFFICIENCY FOR DELIVERY  
POTENTIAL RADIOBIOLOGY IMPLICATIONS  
MOST IMPORTANT IN SBRT***



# SBRT VMAT with FFF in NSCLC Stage I

## PURPOSE

to evaluate preliminary clinical results and pulmonary toxicity

## METHODS AND MATERIALS:

46 patients median age 75 years (58-89 years) M 28 F 12

Stage IA 34 (64%) IB 6 (36%)

CT scan and CT-PET with 18FDG

A pathological diagnoses was available for 18 patients (50%)

Mean CTV: 16 mm

RapidArc with FFF: 4 x 12 Gy

Control group: 86 patients treated with 3DCRT

# SBRT VMAT with FFF in NSCLC Stage I

## PROCEDURE

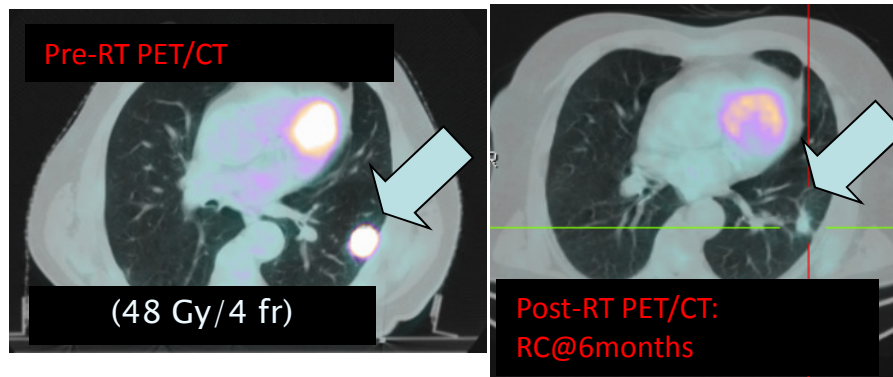
- Thermoplastic masks for the thoracic region
- CT scan from the mandible to the L3 with 3 mm slice thickness in free breathing mode
- 4D-CT scan to evaluate organ motion



## TREATMENT PLANNING

- GTV: lesion
- CTV: Personalized margins in relation to the respiratory motion
- PTV: CTV + 4-5 mm
- Total Dose: 48 Gy in 4 fractions
- CBCT every day

# SBRT VMAT with FFF in NSCLC Stage I



## Toxicity RA-FFF

G1-2: 8/46 patients (17.4%)

G3: 2/46 (4%)

## Toxicity 3DCRT:

G1-2: 21/86 (24.4%)

G3: 8/86 (9%)

| IPSI LUNG | 3DCRT-FF           | VMAT RA - FFF     | p     |
|-----------|--------------------|-------------------|-------|
| V5        | 31.4 % (6.6-57.8)  | 24.9 % (6.8-54)   | 0.02  |
| V20       | 11.8 % (0-26.7)    | 7.3 % (1.2-26.6)  | 0.003 |
| MLD       | 7.2 Gy (0.92-12.6) | 4.8 Gy (1.2-13.3) | 0.001 |

# SBRT VMAT with FFF in NSCLC Stage I

| Time of FU (CT) | PD      | SD       | PR+CR       |
|-----------------|---------|----------|-------------|
| 3 months        |         |          |             |
| •3DCRT          | 6 7.3%  | 28 34%   | 48/82 58.4% |
| •VMAT-RA (FFF)  | -       | 6 15%    | 34/40 85%   |
| 6 months        |         |          |             |
| •3DCRT          | 6 7.3%) | 20 24.3% | 56/82 68.2% |
| •VMAT-RA (FFF)  | -       | 2 5%     | 38/40 95%   |
| 12 months       |         |          |             |
| •3DCRT          | 6 7.3%) | 16 19.5% | 60/82 73%   |
| •VMAT-RA (FFF)  | -       | 2 5%     | 38/40 95%   |

Median FY: 12 months

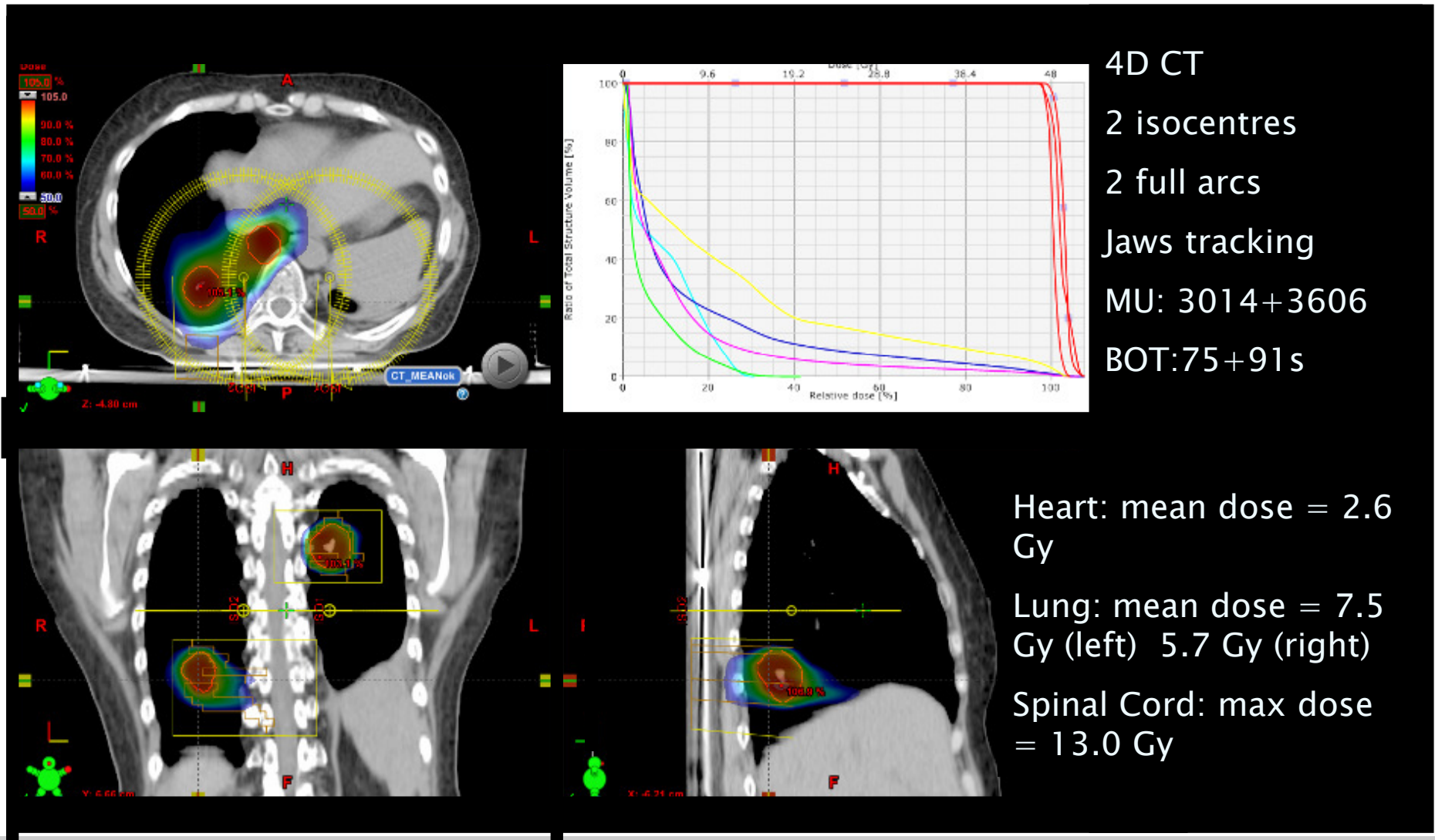
1 yr LC (SD+PR+CR):  
92.5 for 3DCRT  
100% for RA with FFF

6 patients died for other causes.

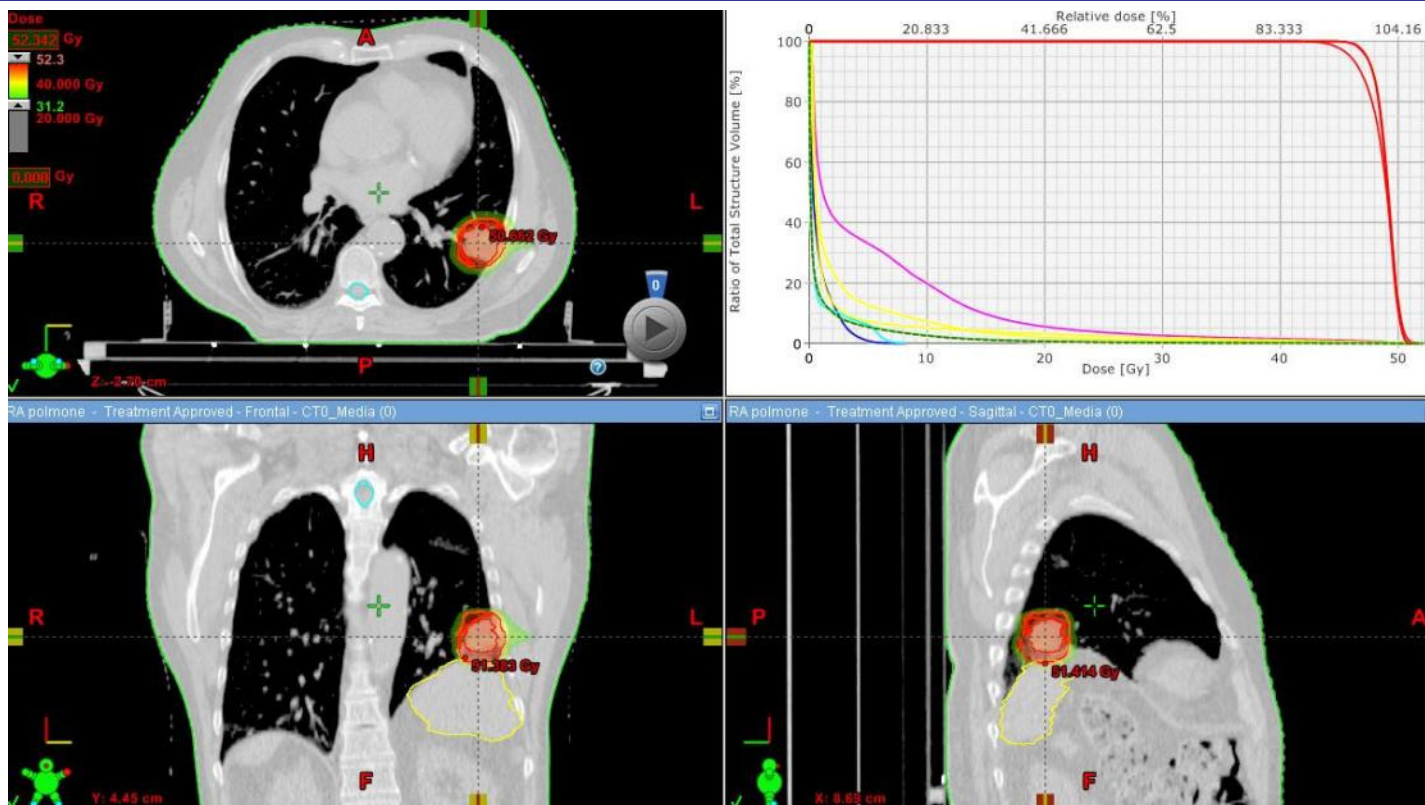
| Time of FU (FDG_PET) | PD     | SD     | PR+CR       |
|----------------------|--------|--------|-------------|
| 12 months            |        |        |             |
| •3DCRT               | 6 9.7% | 4 6.5% | 52/62 83.8% |
| •VMAT-RA (FFF)       | -      | -      | 34/34 100%  |

Crude OS = 87%  
OS (tumor related) = 100%

# SBRT in lung: 12Gyx4;10FFF;DR 2400.



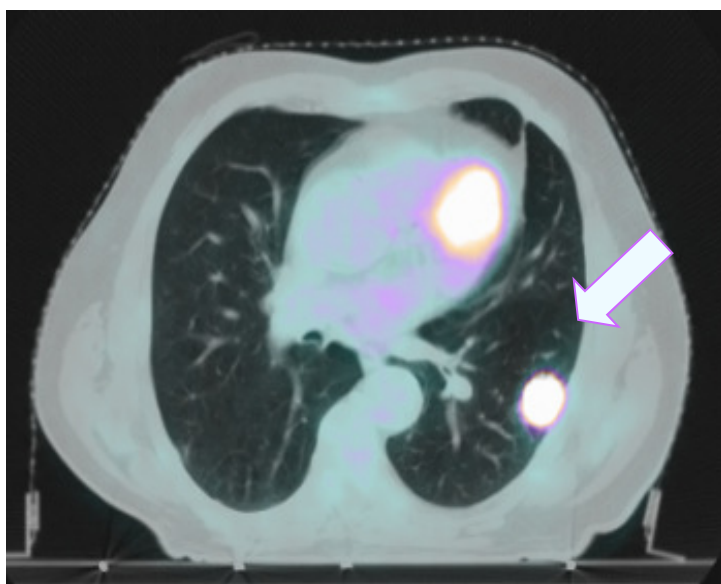
# Male 76 years NSCLC Stage IA - 48 Gy/4 fr



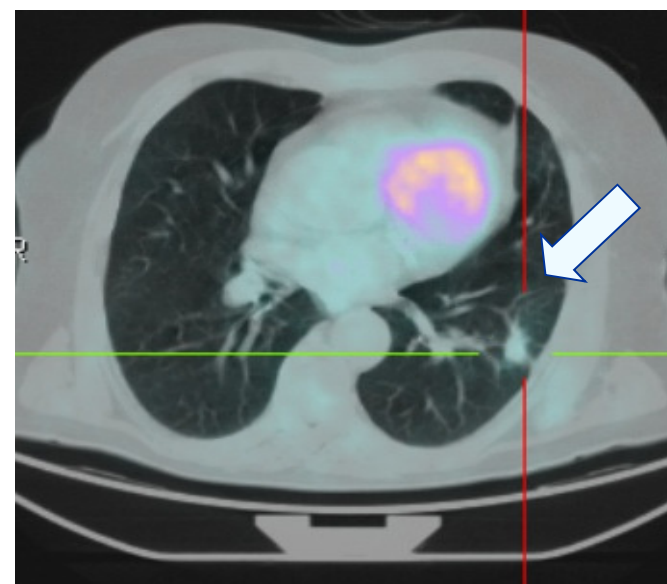
Median beam on time (BOT) was reduced by 75% passing from about 8 minutes (with FF modality) to 2 minutes (with FFF modality):  
Increased of patient comfort and Reduction of intra-fraction motion

# Male 76 years NSCLC Stage IA - 48 Gy/4 fr

Pre SBRT



Post SBRT



RESPONSE: COMPLETE REMISSION PET- CT AT 6 MONTHS

# RapidArc, TB and FFF in prostate: scientific literature

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Scientific Literature RapidArc® TrueBeam™  
and other advanced Varian Capabilities

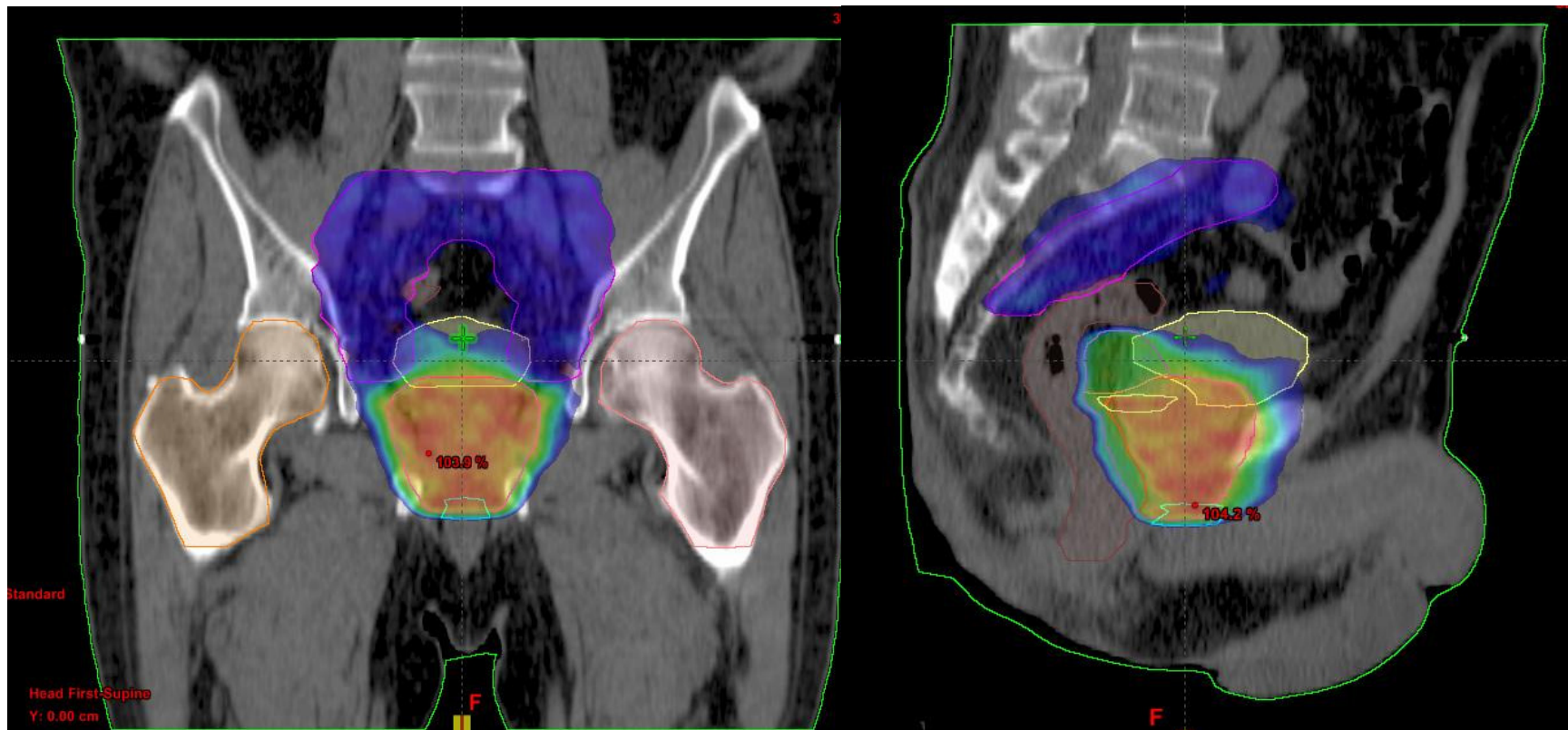


Shaffer et al. Clin. Oncol. 2008  
Palma et al. IJROBP 2008  
Kjaer et al. Acta Oncol. 2009  
**Weber et al. Radiat. Oncol. 2009**  
Yoo et al. IJROBP 2010  
Pesce et al. Radiat. Oncol. 2010  
Jacob et al. Strahl. Onkol. 2010  
Aznar et al. Radiother. Oncol. 2010  
Reggiori et al. JACMP 2011  
Jolly et al. JACMP 2011  
Fogarty et al. Radiat. Oncol. 2011  
Oliver et al. JACMP 2011  
Sze et al Med. Dosim. 2012  
Zwahlen et al. IJROBP 2012  
Alongi et al. Strahl. Onkol. 2012



# Prostate with RA-SIB

74 Gy T – 66 Gy VS - 50 Gy LN



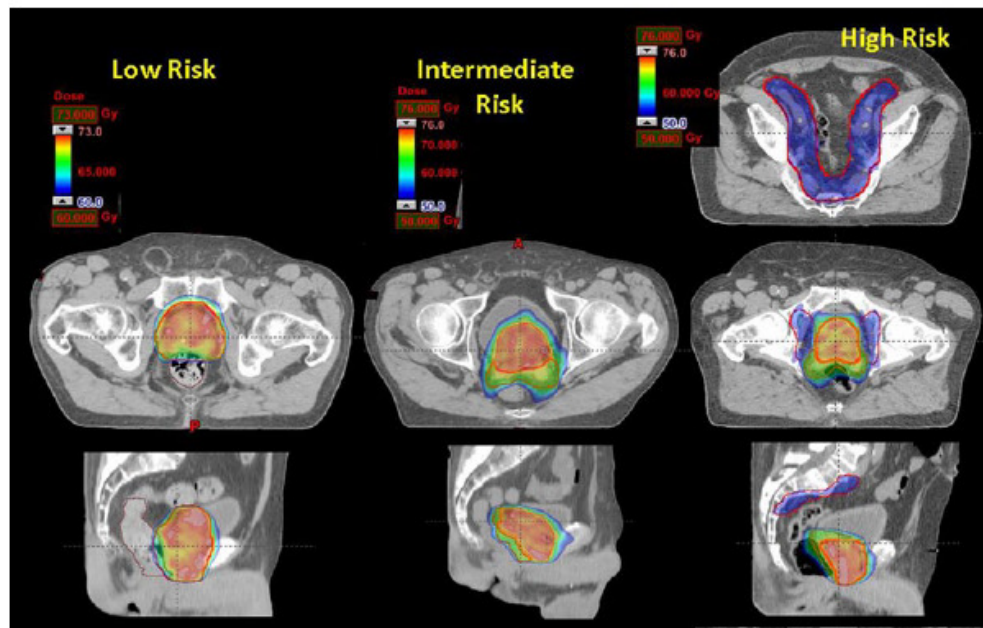
# Moderate hypofractionation

F. Alongi<sup>1</sup> · A. Fogliata<sup>2</sup> · P. Navarria<sup>1</sup> · A. Tozzi<sup>1</sup> · P. Mancosu<sup>1</sup> · F. Lobefalo<sup>1</sup> · G. Reggiori<sup>1</sup> · A. Clivio<sup>2</sup> · L. Cozzi<sup>2</sup> · M. Scorsetti<sup>1</sup>

<sup>1</sup> Department of Radiotherapy, Humanitas Cancer Center, Istituto Clinico Humanitas, Rozzano, Milan

<sup>2</sup> Medical Physics Unit, Oncology Institute of Southern Switzerland, Bellinzona

## Moderate hypofractionation and simultaneous integrated boost with volumetric modulated arc therapy (RapidArc) for prostate cancer



All patients were treated in 28 fractions with a moderate hypofractionated schedule:

- low-risk patients received 71.4 Gy to PTV1, i.e., 2.55 Gy/fraction (5 patients also had seminal vesicles (PTV2) irradiation up to 65.5 Gy),
- intermediate-risk patients received 74.2 Gy to PTV1, i.e., 2.65 Gy/fraction and 61.6 or 65.5 Gy to PTV2 exceeding PTV1 (seminal vesicles), and
- high-risk patients received 74.2 Gy to PTV1 (prostate), 61.6 or 65.5 Gy to PTV2 exceeding PTV1 (seminal vesicles), and 51.8 Gy to PTV3 exceeding PTV2 (pelvic lymph nodes).

**Tab. 1** Demographic and acute toxicity results

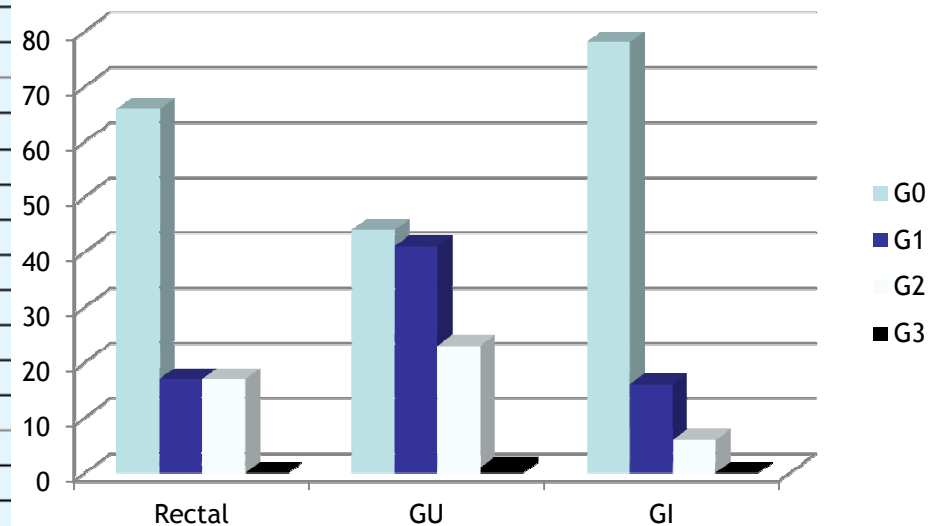
|               |                | Low risk   | Intermediate risk | High risk   | All        |
|---------------|----------------|------------|-------------------|-------------|------------|
| Age (years)   | Median (range) | 75 (60–79) | 75 (60–84)        | 74 (62–82)  | 75 (60–84) |
| Stage         | Patients (n)   | 25         | 34                | 11          | 70         |
| Gleason score | Median (range) | 6 (4–8)    | 7 (4–9)           | 8 (6–10)    | 7 (4–10)   |
| Initial PSA   | Median (range) | 6.3 (3–10) | 5.8 (3–44)        | 23.6 (7–40) | 6.8 (3–44) |

# Acute Toxicity profile from moderate hypofractionation (70 patients)

- 74.2 Gy in 2.65Gy/fr prescribed in 78% of pts (intermediate and high risk)
- 71.4Gy in 2.55Gy/fr prescribed in 22% of pts (low risk)

|                          |                | Low risk    | Intermediate risk | High risk   | All         |
|--------------------------|----------------|-------------|-------------------|-------------|-------------|
| Age (years)              | Median (range) | 75 (60–79)  | 75 (60–84)        | 74 (62–82)  | 75 (60–84)  |
| Stage                    | Patients (n)   | 25          | 34                | 11          | 70          |
| Gleason score            | Median (range) | 6 (4–8)     | 7 (4–9)           | 8 (6–10)    | 7 (4–10)    |
| Initial PSA              | Median (range) | 6.3 (3–10)  | 5.8 (3–44)        | 23.6 (7–40) | 6.8 (3–44)  |
| <b>Rectal toxicity</b>   |                |             |                   |             |             |
| Patients, n (%)          | Grade 0        | 18/25 (72%) | 22/34 (65%)       | 6/11 (55%)  | 46/70 (66%) |
|                          | Grade 1        | 2/25 (8%)   | 7/34 (21%)        | 3/11 (27%)  | 12/70 (17%) |
|                          | Grade 2        | 5/25 (20%)  | 5/34 (15%)        | 2/11 (18%)  | 12/70 (17%) |
|                          | Grade 3        | 0/25 (0%)   | 0/34 (0%)         | 0/11 (0%)   | 0/70 (0%)   |
| <b>GU toxicity</b>       |                |             |                   |             |             |
| Patients, n (%)          | Grade 0        | 10/25 (40%) | 17/34 (50%)       | 4/11 (36%)  | 31/70 (44%) |
|                          | Grade 1        | 7/25 (28%)  | 11/34 (32%)       | 4/11 (36%)  | 22/70 (31%) |
|                          | Grade 2        | 7/25 (28%)  | 6/34 (18%)        | 3/11 (27%)  | 16/70 (23%) |
|                          | Grade 3        | 1/25 (4%)   | 0/34 (0%)         | 0/11 (0%)   | 1/70 (1%)   |
| <b>Upper GI toxicity</b> |                |             |                   |             |             |
| Patients, n (%)          | Grade 0        | 22/25 (88%) | 26/34 (76%)       | 6/10 (60%)  | 54/69 (78%) |
|                          | Grade 1        | 2/25 (8%)   | 6/34 (18%)        | 3/10 (30%)  | 11/69 (16%) |
|                          | Grade 2        | 1/25 (4%)   | 2/34 (6%)         | 1/10 (10%)  | 4/69 (6%)   |
|                          | Grade 3        | 0/25 (0%)   | 0/34 (0%)         | 0/10 (0%)   | 0/69 (0%)   |

PSA prostate-specific antigen, GU genitourinary, GI gastrointestinal.

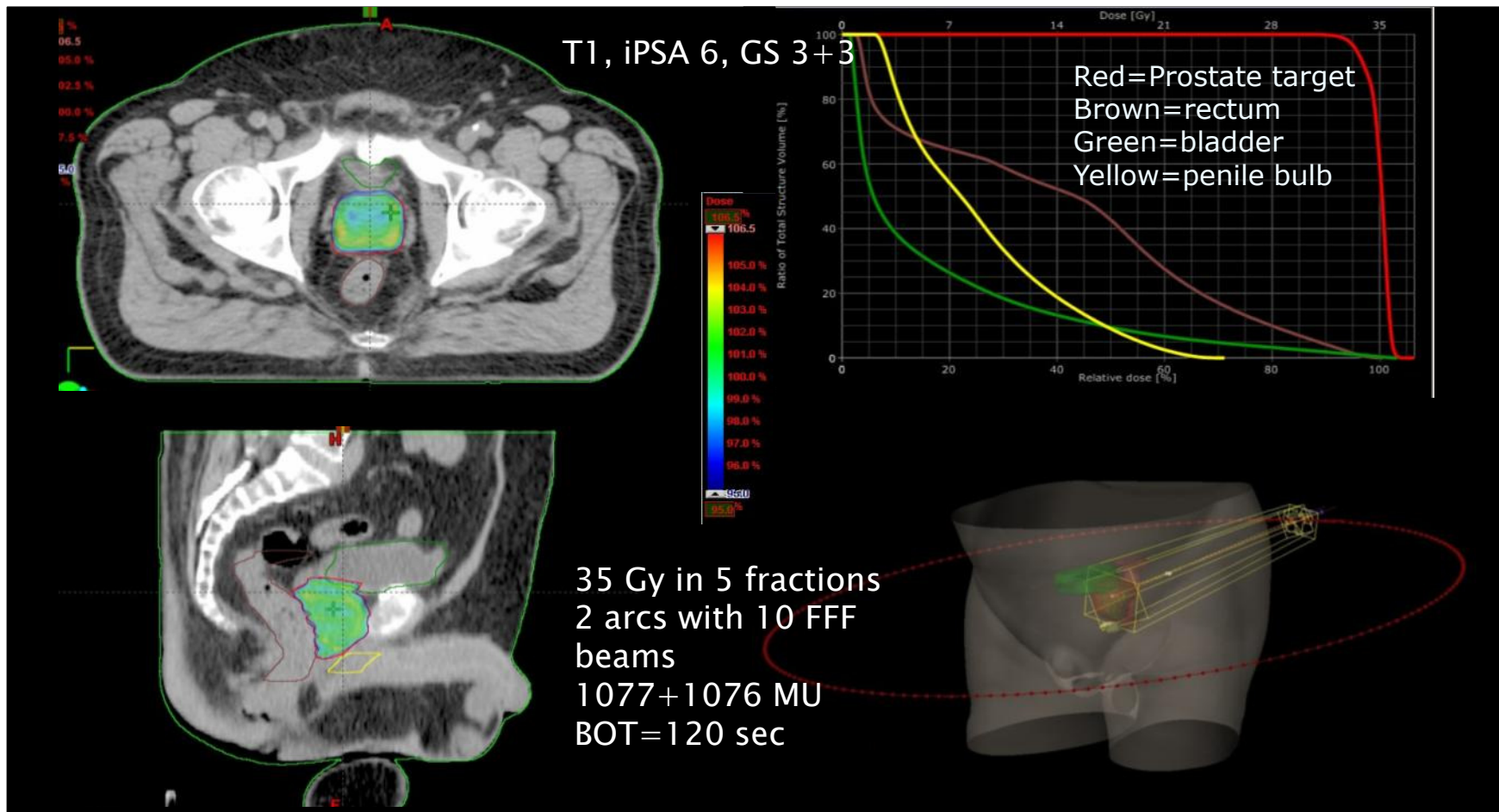


# Extreme Hypofractionation on TB: Phase II trial

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- Age  $\leq$  80 years
- WHO performance status  $\leq$  2.
- Histologically proven prostate adenocarcinoma  $\rightarrow$  Any case where prophylactic lymph node irradiation is not required (risk of microscopic involvement  $\leq$  15%)
- PSA  $\leq$  20 ng/ml.
- T1–T2 (localized)–stage
- No pathologic lymph nodes at CT/ MR and NO distant metastases
- No previous prostate surgery other than TURP
- No malignant tumors in the previous 5 years
- IPSS 0–7
- Combined HT according to risk factors.
- Informed consent

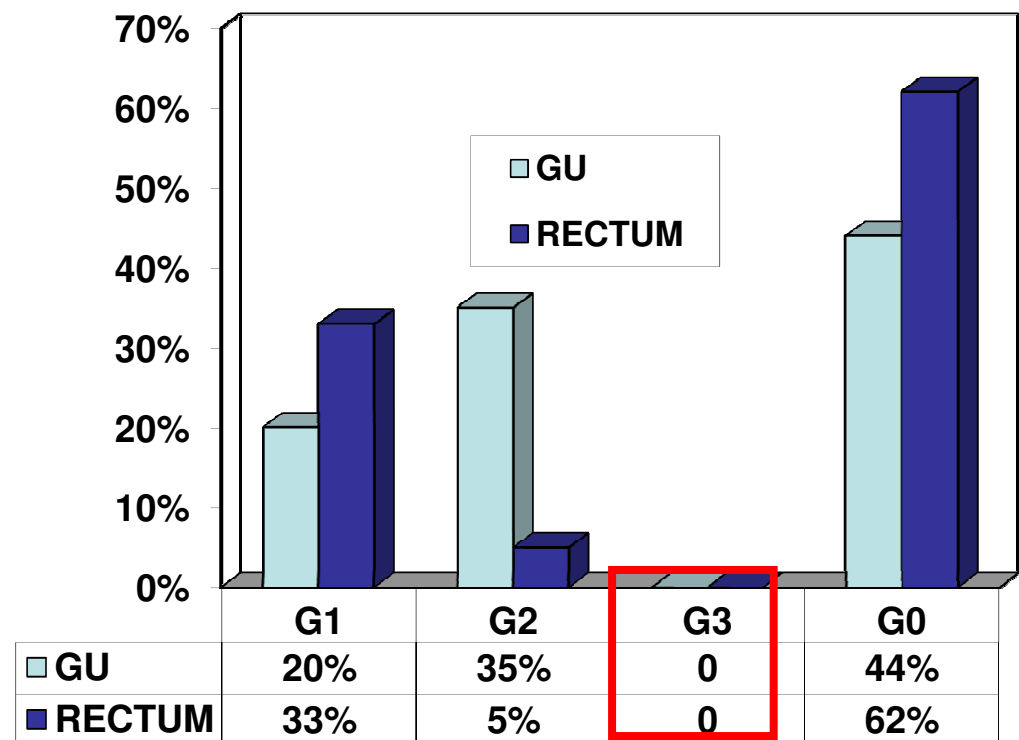
# Extreme Hypofractionation on TB: Phase II trial



Submitted, confidential

# Extreme Hypofractionation on TB: Phase II trial

|                          |                      |
|--------------------------|----------------------|
| N Patients recruited     | 34                   |
| GS (median)              | 6(6-7)               |
| iPSA (median)            | 6(0.50-12)           |
| Dose prescribed          | 35 Gy in 5 fractions |
| BOT(median)              | 106(64-120)          |
| Duration in days(median) | 11.8(9-22)           |
| F-UP(median)             | 5(1-9)               |
| N SPACEOAR               | 9 implants           |



ESTRO 2013 Accepted

# LIVER: SBRT with RapidArc and FFF

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## Liver:

Yin et al. Med. Dosim. 2011

Viellot et al. Radiat. Oncol. 2011

Kuo et al. Radiat. Oncol. 2011

Reggiori et al. Med. Phys. 2012

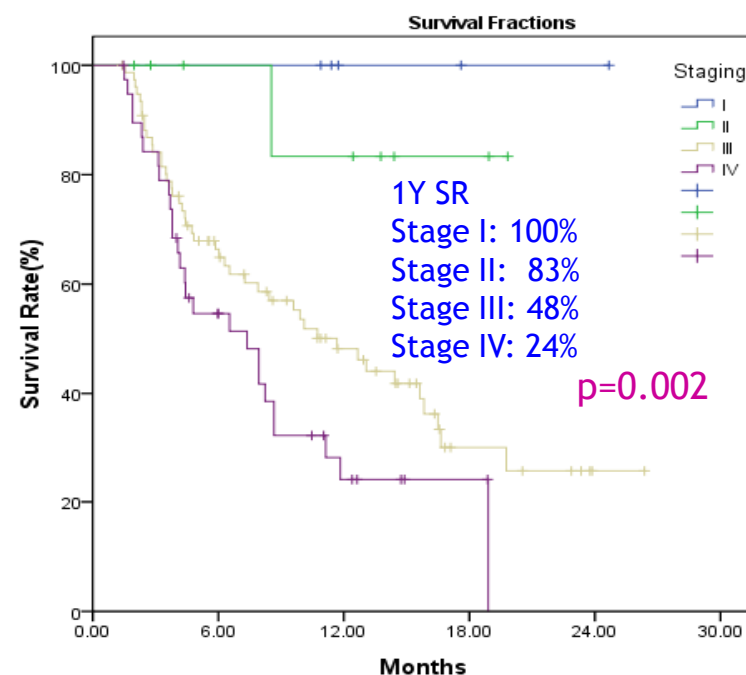
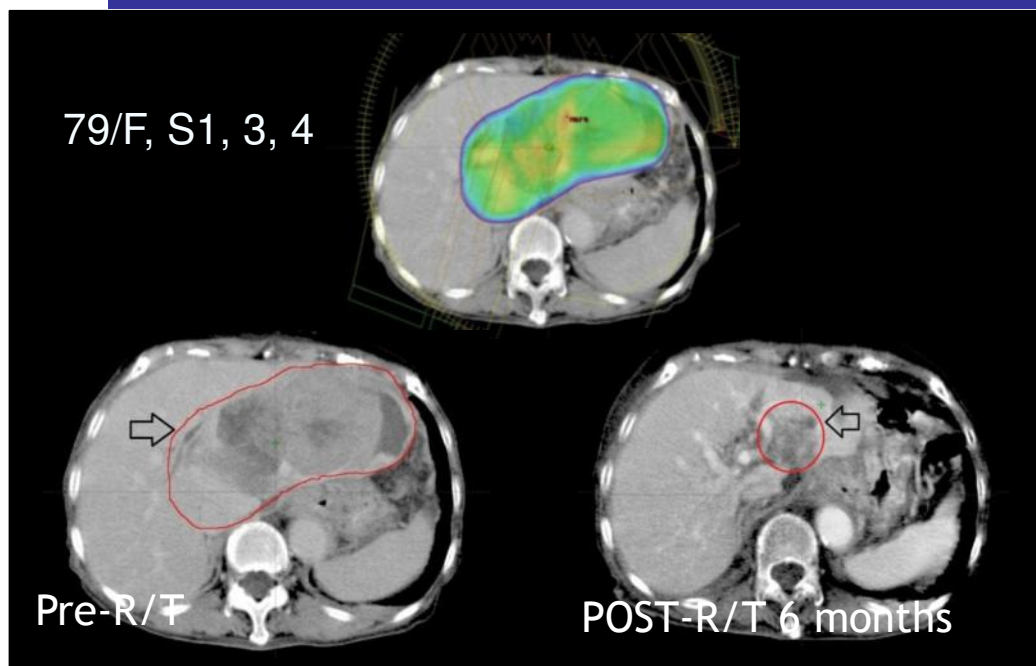
Gong et al. Strahl. Onko. 2012

Mancosu et al. Radiat. Oncol. 2012

Wang et al. STO 2012 at press

Wang et al. Radiat. Oncol. 2012

# Primary hepatic ca: Preliminary Results on 138pts



- Response rate: 65%
- 1 Y survival rate: 45.5%
- Mean survival: 13.5 mo
- RILD: G1-2: 24, (18%); G3-4: 10 (7%)



# Primary hepatic ca: Phase I-II monoinstitutional trial.

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Risk adaptive fractionation regimen

For tumor size <3cm and good liver reserve:

15-20Gy \* 3 fractions

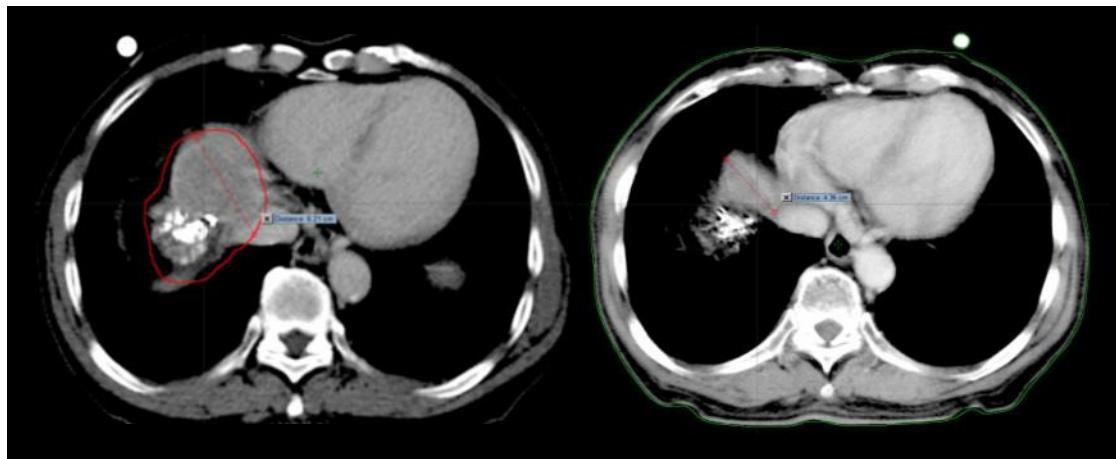
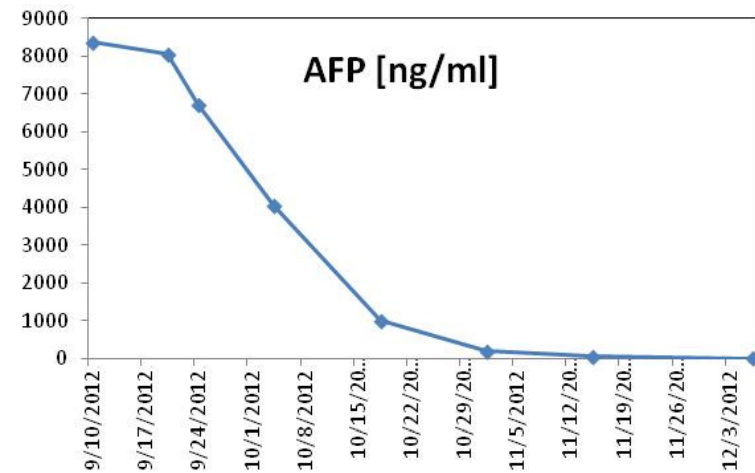
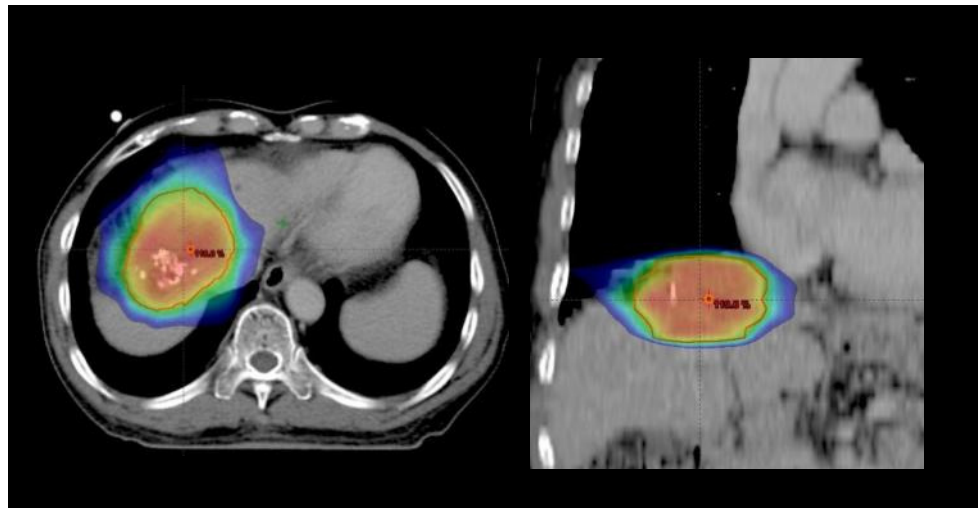
For tumor size between 3-5cm or not enough liver reserve:

8-12Gy\*5 fractions

For tumor size more than 5 cm:

5-5.5Gy\*10 fractions

# Primary hepatic ca: moderate hypofractionation



70 yo man,  
T3bN0M0 (stage IIIB), Okuda stage I,  
BCLC stage C, Child-Pugh stage A

55 Gy in 10 fractions  
RA with TB. 10MV FFF. ~90 seconds

# Liver Metastases: Rationale for SABR

**Table 3.** Prospective Trials of Stereotactic Body Radiation Therapy for Hepatic Metastases

| Study                             | No. of Lesions | Fractionation          | Median Follow-Up | Actuarial Local Control |    |
|-----------------------------------|----------------|------------------------|------------------|-------------------------|----|
|                                   |                |                        |                  | Time                    | %  |
| Herfarth et al <sup>16</sup>      | 55             | 1 × 14 Gy to 1 × 26 Gy | 6 months         | 18 months               | 67 |
| Hoyer et al <sup>24</sup>         | 141*           | 3 × 15 Gy              | 4.3 years        | 2 years                 | 79 |
| Milano et al <sup>21</sup>        | 293†           | 10 × 5 Gy              | 41 months‡       | 2 years                 | 67 |
| Mendez-Romero et al <sup>25</sup> | 45             | 3 × 12.5 Gy§           | 13 months        | 2 years                 | 82 |
| Rusthoven et al (this study)      | 49             | 3 × 20 Gy              | 16 months        | 2 years                 | 82 |

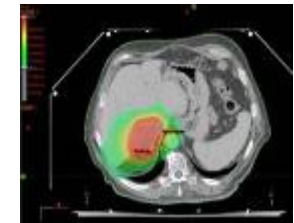
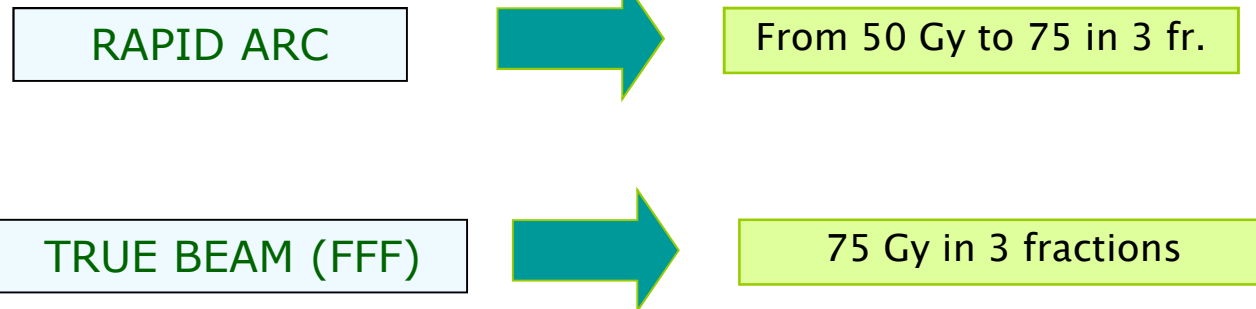
\*Total number of colorectal cancer metastases; 44 liver metastases.

†Total number of lesions treated; 45% of patients were treated for hepatic metastases.

‡In surviving patients.

§Different fractionation (3 × 10 Gy or 5 × 5 Gy) used for patients with hepatocellular carcinoma or with lesions ≥ 4 cm.

## Liver metastasis treatment in ICH Radioablation



# Prospective Phase II study of Stereotactic Body Radiation Therapy (SBRT) for liver metastases

## END POINTS

- PRIMARY: in field local control
- SECONDARY: toxicity (CTCAE3), progression-free survival and overall survival

## INCLUSION CRITERIA

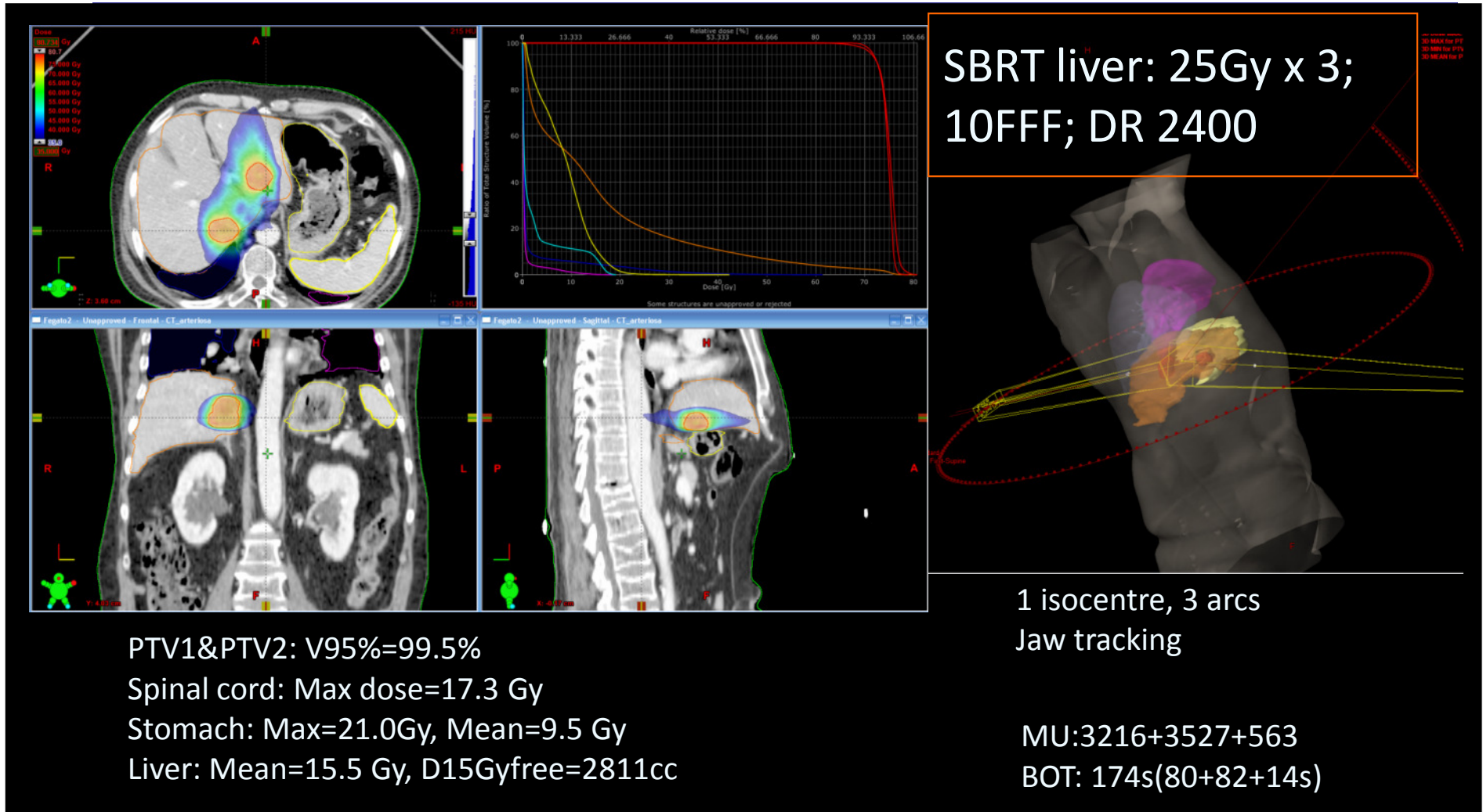
- Inoperable or medically unsuitable for resection
- Maximum tumour diameter < 6cm
- $\leq 3$  discrete lesions
- Performance status 0-2
- Good compliance to treatment

# Prospective Phase II study of Stereotactic Body Radiation Therapy (SBRT) for liver metastases

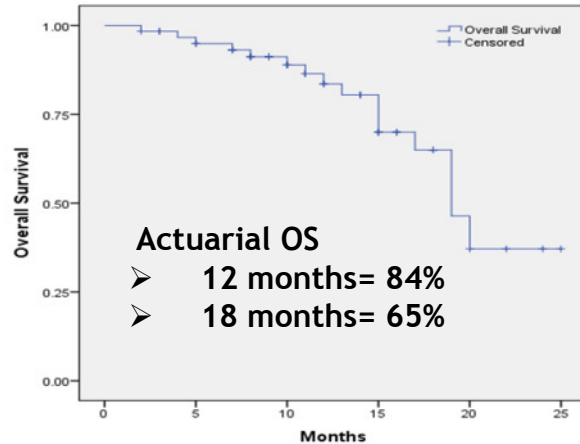
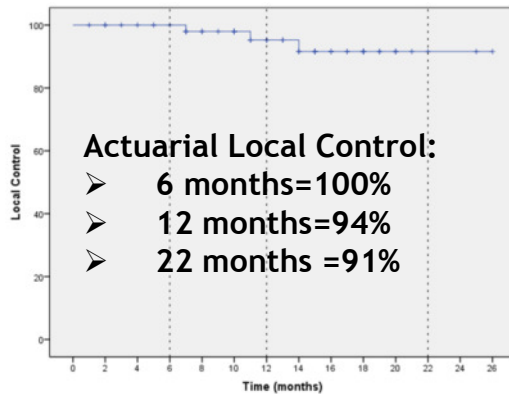
| Patients characteristics     | Value  | Treatment characteristics  | Value  |
|------------------------------|--|----------------------------|--|
| <b>No. of patients</b>       | <b>61</b>  | <b>No. of lesions</b>      | <b>76</b>  |
| Age (y)                      | 65 (range 39 – 87)                               | Diameter < 3cm             | 45 (60%)   |
| Sex (male:female)            | 26:35  | Diameter > 3cm             | 31 (40%)   |
| Baseline KPS                 | > 90   | No. of lesions per patient | 1 for 48 pts (79%)<br>2 for 11 pts (18%)<br>3 for 2 pts (3%) |
| Prior liver-directed therapy | 21% (12 pts)                                     |                            |  |
| Primary site                 | 29 Colon<br>11 Breast<br>7 Gyn<br>14 Other sites |                            |  |
| Extrahepatic disease         | 34% (21 pts)                                     |                            |  |

|                   | Total Dose      |                 |
|-------------------|-----------------|-----------------|
| <b>Full</b>       | <b>75 Gy</b>    | <b>55 (72%)</b> |
| <b>Dose - 10%</b> | <b>67.5 Gy</b>  | <b>6 (8%)</b>   |
| <b>Dose - 20%</b> | <b>61.89 Gy</b> | <b>4 (5%)</b>   |
| <b>Dose - 30%</b> | <b>56.25 Gy</b> | <b>11 (14%)</b> |

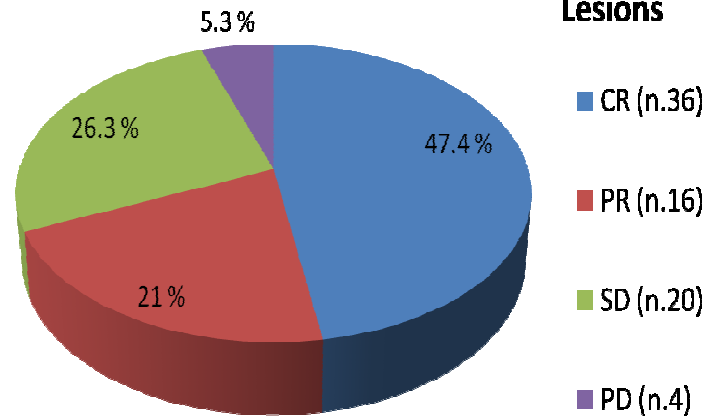
# SABR for liver mets with FFF beams



# Humanitas: SABR for metastatic liver (RA with FFF): IJROBP 2013



**Pattern of response**



**ACUTE TOXICITY:**

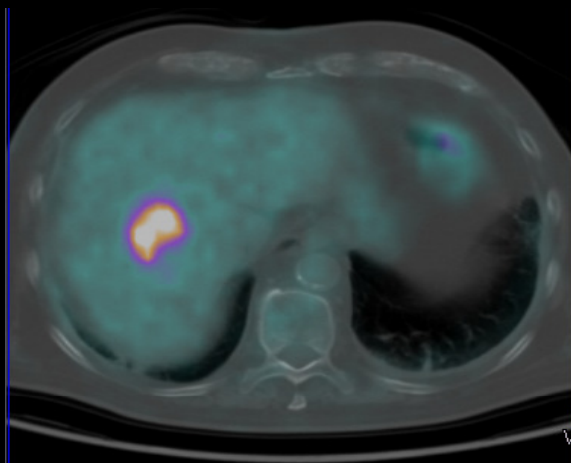
- G2 toxicity 4 %
- G2 transient transaminase increase 26%
- No G3-G4 or G5 toxicity observed

**NO RILD**

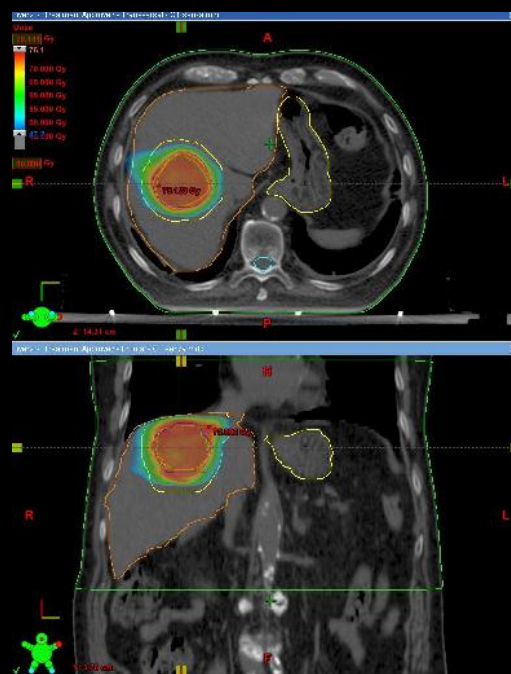
**Median OS rate was 19 months**

# FU: SBRT 25Gy x 3; 10FFF; DR 2400.

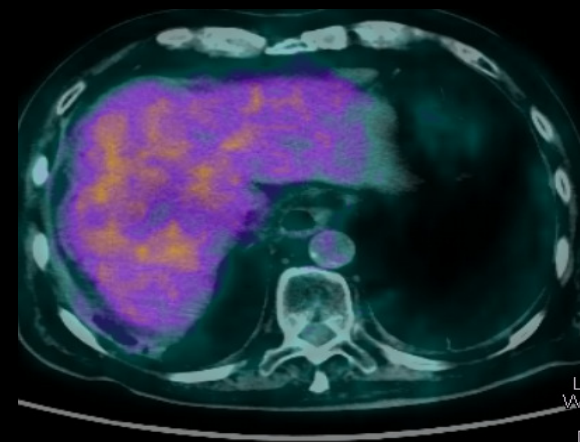
PET pre



RapidArc  
1 isocentre  
2 arcs  
Jaw tracking



PET after 6 months

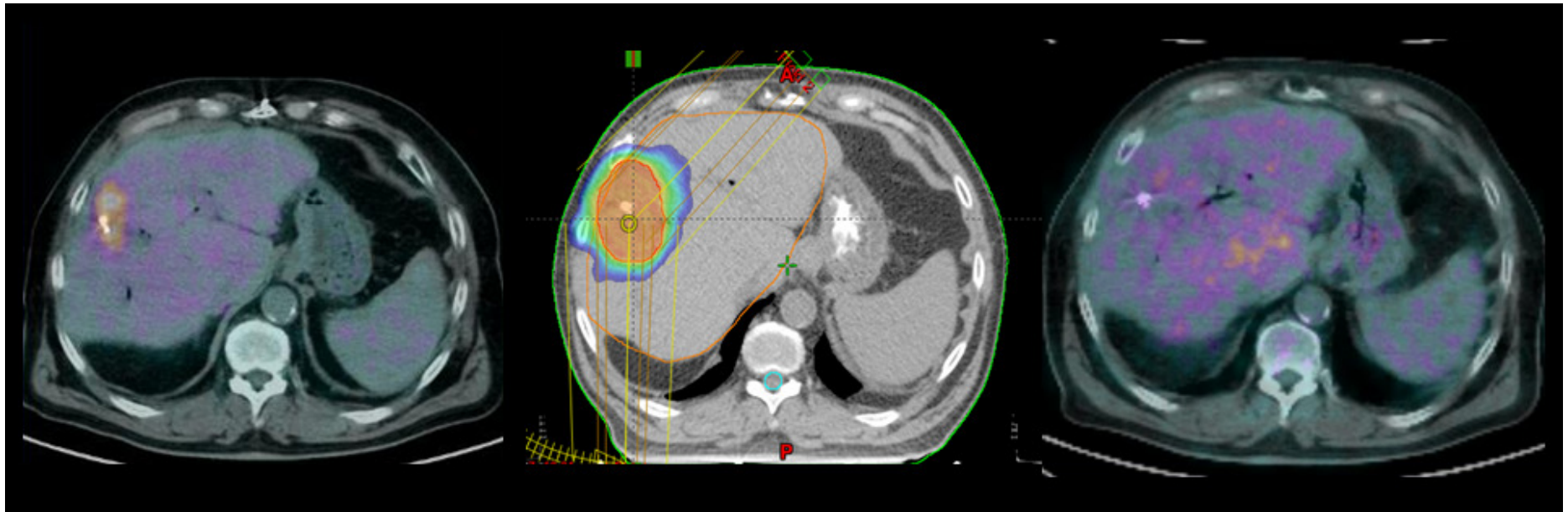


MU: 2953+2955  
BOT: 150 sec



# SABR 25Gy x 3; 10FFF; DR 2400.

Patient treated with SBRT for local relapse after hepatic surgery for colorectal metastasis



PET -CT pre-treatment,  
CEA 72

PET -CT post-treatment  
CEA 2.2

**Thank you for your interest  
and attention**



eoc

