

**Il trattamento VMAT con alto dose rate (FFF): offerta tecnologica,
applicazioni cliniche e implicazioni radiobiologiche**



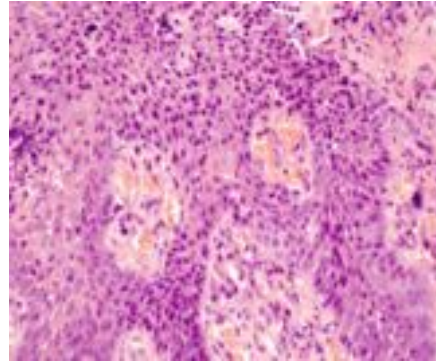
Dr.ssa Marta Scorsetti

Radioterapia e Radiochirurgia

Istituto Clinico Humanitas

VMAT-Flattening Filter Free

1. Radiobiology



2. Available Technology



3. Clinical applications

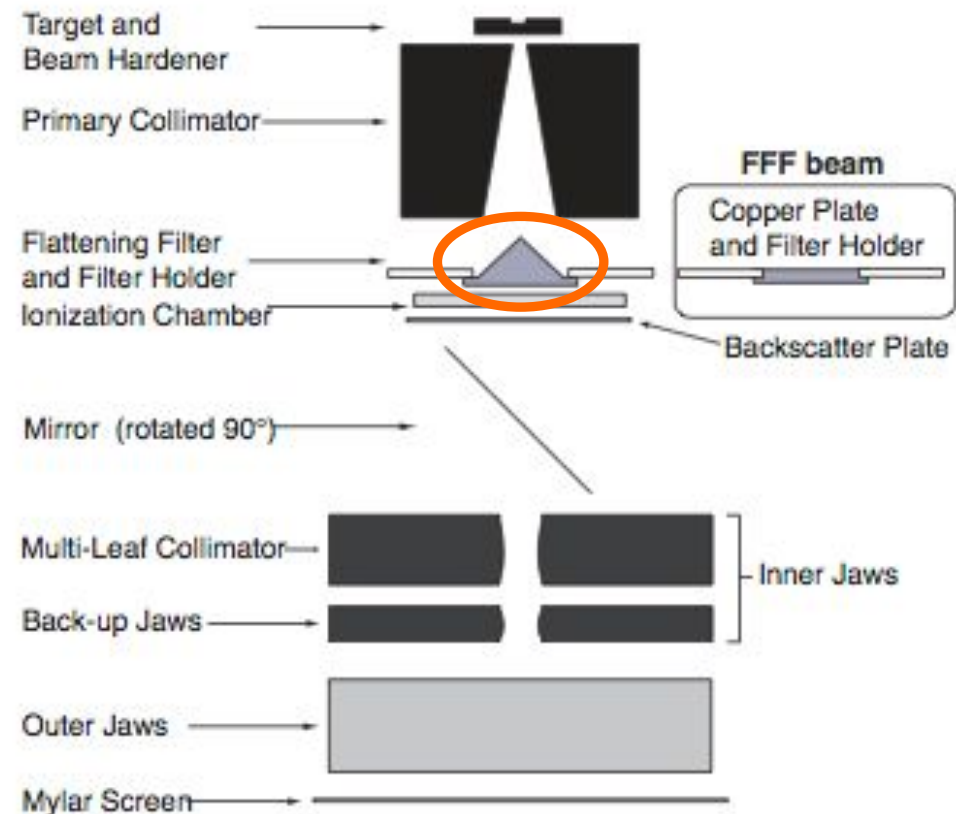


Flattening Filter Free beam

Flattening filters FFs have been considered as an **integral part of the treatment head of a medical accelerator** for more than 50 years.

Advanced treatment techniques, such as **stereotactic radiotherapy or intensity modulated radiotherapy** have stimulated the **interest in operating linear accelerators in a flattening filter free FFF mode.**

In the 1990s, several groups studied flattening filter free (FFF) **high-energy photon beams.**



Georg 2011

Radiobiology



Current status and future perspective of flattening filter free photon beams^{a)}

Dietmar Georg,^{b)} Tommy Knöös, and Brendan McClean
Department of Radiotherapy, Division of Medical Radiation Physics, Medical University of Vienna/AKH Vienna, A-1090 Vienna, Austria; Department of Physics, St. Luke's Hospital, Highfield Rd., Rathgar, Dublin 6, Ireland; and Radiation Physics, Lund University and Skåne University Hospital, S-221 85 Lund, Sweden

A number of dosimetric benefits have been determined for FFF beams:

- ✓ significant decrease in treatment times by increasing the instantaneous dose-rate of the accelerator
- ✓ reduced head scatter
- ✓ reduction in the out-of-field dose

Radiobiology



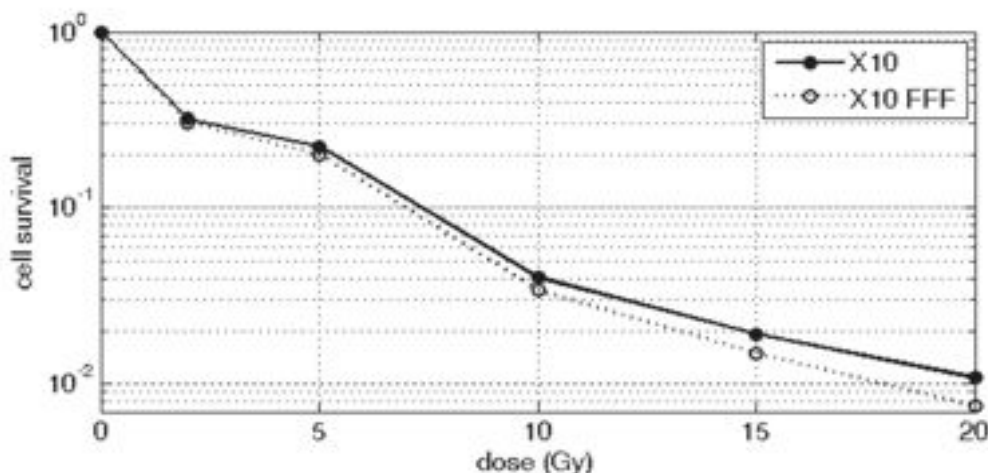
Dose rate

Effect of high dose per pulse flattening filter-free beams on cancer cell survival

Ines Lohse^a, Stephanie Lang^a, Jan Hrbacek^a, Stephan Scheidegger^c, Stephan Bodis^b, Nadia S. Macedo^a, Jianhua Feng^a, Urs M. Lütolf^a, Kathrin Zaugg^{a,*}

^a Department of Radiation Oncology, University Hospital Zürich, Switzerland; ^b Institute of Radiation Oncology, Kantonsspital Aarau, Switzerland; ^c Centre of Applied Mathematics and Physics, Zurich University of Applied Science, Switzerland

Results: The results presented here demonstrate **that irradiation of glioblastoma cell lines using the FFF beam is more efficient in reducing clonogenic cell survival** than the standard flattened beam, an effect which becomes **more significant the higher the single dose**. Interestingly, in our experimental setting, the radiobiological effect of the FFF beam is dependent on dose per pulse rather than on delivery time.



Dose–response curve of U87-MG cells irradiated with either the X10 (full circles) or X10FFF (empty circles) beam. Clonogenic survival was accessed as a measure for irradiation efficiency.

** $p \leq 0.001$.

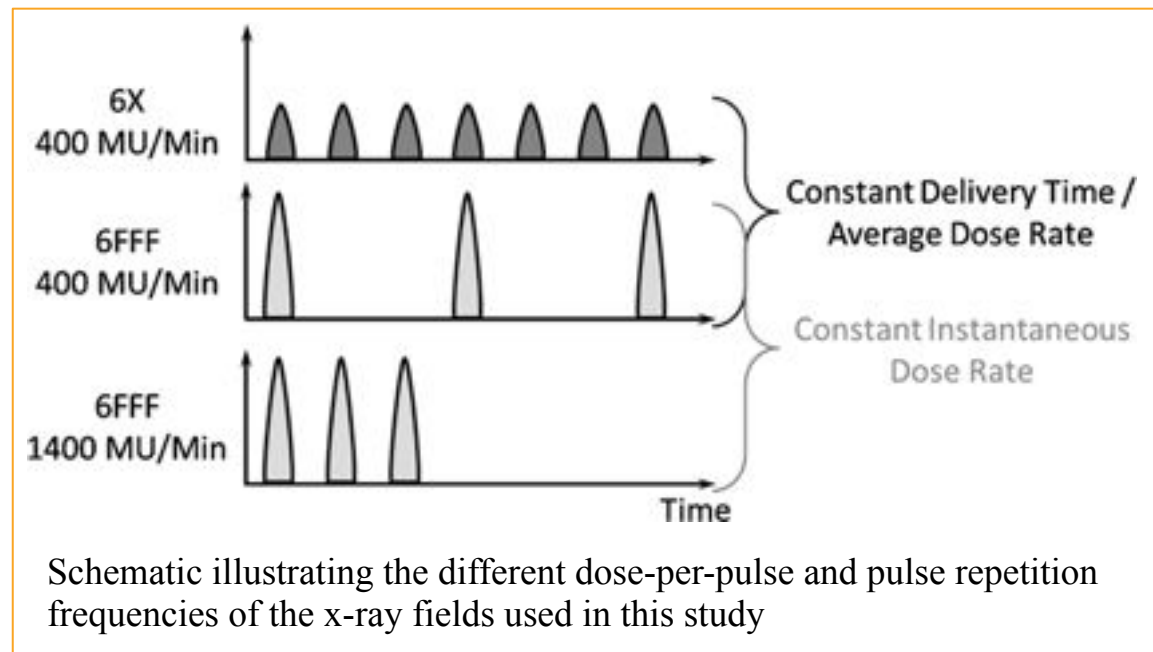
Radiobiology

An *in vitro* study of the radiobiological effects of flattening filter free radiotherapy treatments

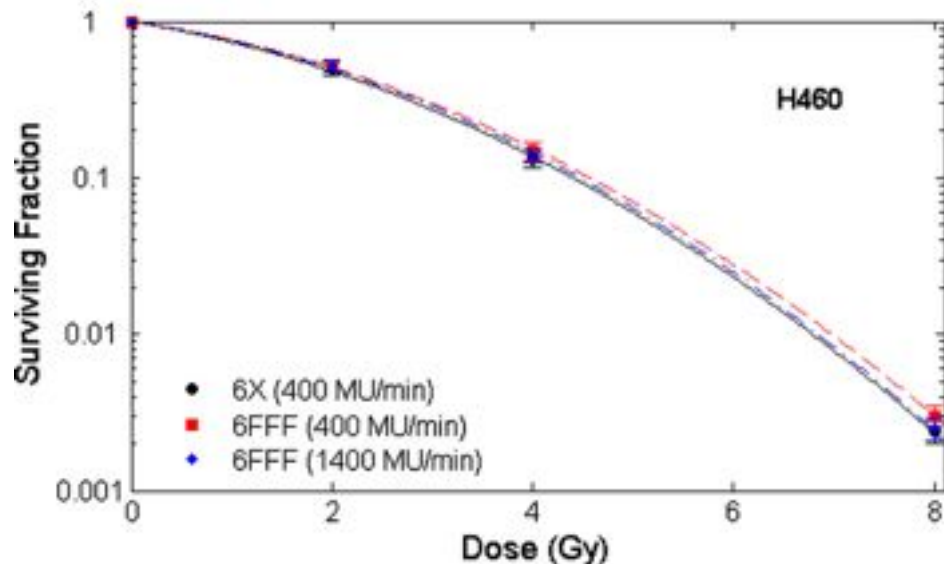
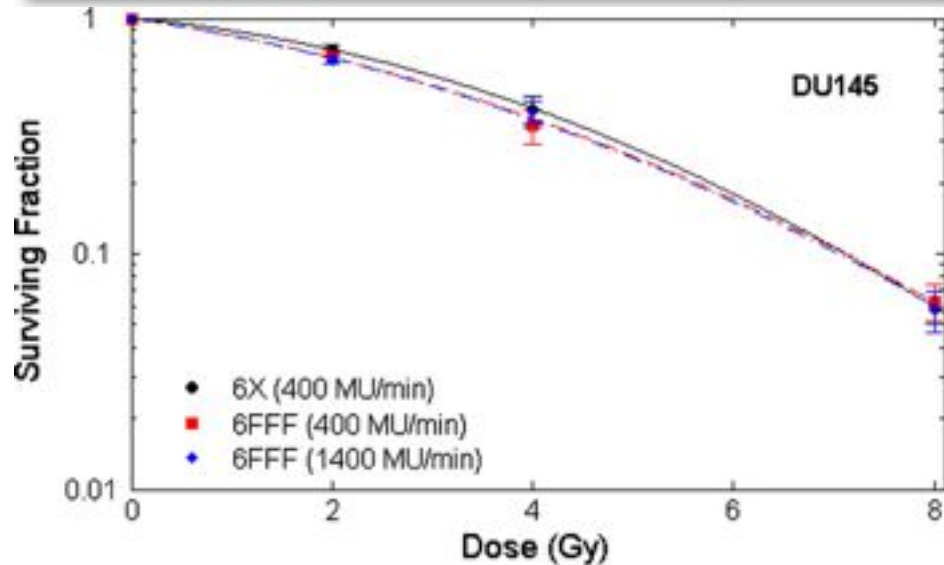
R B King¹, W B Hyland¹, A J Cole^{2,3}, K T Butterworth³,
S J McMahon³, K M Redmond³, C Trainer³, K M Prise³,
C K McGarry¹ and A R Hounsell^{1,3}

2013

To determine the radiobiological impact of the increased dose-rates from FFF exposures a Varian Truebeam medical linear accelerator was used to **irradiate two human cancer cell lines in vitro, DU-145 prostate and H460 non-small cell lung, with both flattened and FFF 6 MV beams.**



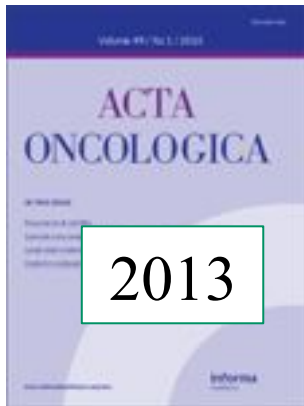
Radiobiology



The results indicate that collective damage behaviour does not occur at the instantaneous dose-rates investigated here and that the use of either modality should result in the **same clinical outcome**, however this will require further validation *in vivo*.

Flattening filter-free treatments **offer many clinical advantages** over the traditional flattened treatments, including **significantly faster delivery of dose fractions**.

Radiobiology



Comparable cell survival between high dose rate flattening filter free and conventional dose rate irradiation

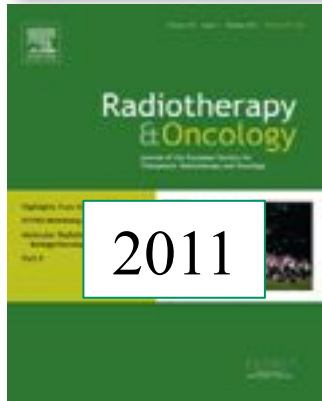
WILKO F. A. R. VERBAKEL^{1,2}, JAAP VAN DEN BERG¹, BEN J. SLOTMAN¹ & PETER SMINIA¹

¹Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands, and ²Department of Physics and Medical Technology, VU University Medical Center, Amsterdam, The Netherlands

Material and methods The human **astrocytoma** D384, **glioma** T98 and **lung carcinoma** SW1573 cell lines were irradiated using either a single dose (0 – 12 Gy) or a fractionated protocol of 5 daily fractions of 2 Gy (D384) or 3 Gy (SW1573).

Conclusion FFF irradiation with a dose rate of 2400 MU/min and four times higher dose per pulse compared to irradiation with FF beams **did not change cell survival** for three human cancer cell lines up to a fraction dose of 12 Gy compared to irradiation using FF beams.

Radiobiology



Dose rate

Dependence of cell survival on instantaneous dose rate of a linear accelerator

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^aDepartment of Experimental Clinical Oncology; and ^bDepartment of Medical Physics, Aarhus University Hospital, Denmark

Materials and methods: A Varian Trilogy TX linear accelerator was used to directly compare the effect of three different dose rates (5.01, 9.99 and 29.91 Gy/min, with instantaneous dose rates in the pulse of 56.5, 112.8 and 338 Gy/s) on clonogenic survival. V79 and FaDu_{DD} cells were irradiated with doses in a range from 1 to 10 Gy in order to obtain dose response curves.

Results: For both cell lines, there is **not observed any effect of the instantaneous dose rate on cell survival.**

Available Technology

2002



2001



The helical Tomotherapy unit and the Cyberknife are two more recent developments of treatment units without a flattening filter.

Available Technology

2012



Elekta HD Versa

**6MV 16Gy/min
10MV 22Gy/min**

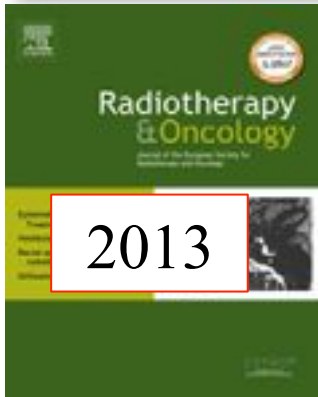
2010



VARIAN TrueBeam

**6MV 14 Gy/min
10MV 24 Gy/min**

Clinical Applications



Stereotactic radiotherapy

Clinical application of flattening filter free beams for extracranial stereotactic radiotherapy

Stephanie Lang, Binaya Shrestha, Shaun Graydon, Frederique Cavelaars, Claudia Linsenmeier, Jan Hrbacek, Stephan Klöck, Gabriela Studer, Oliver Riesterer *

Department of Radiation Oncology, University Hospital Zurich, Switzerland

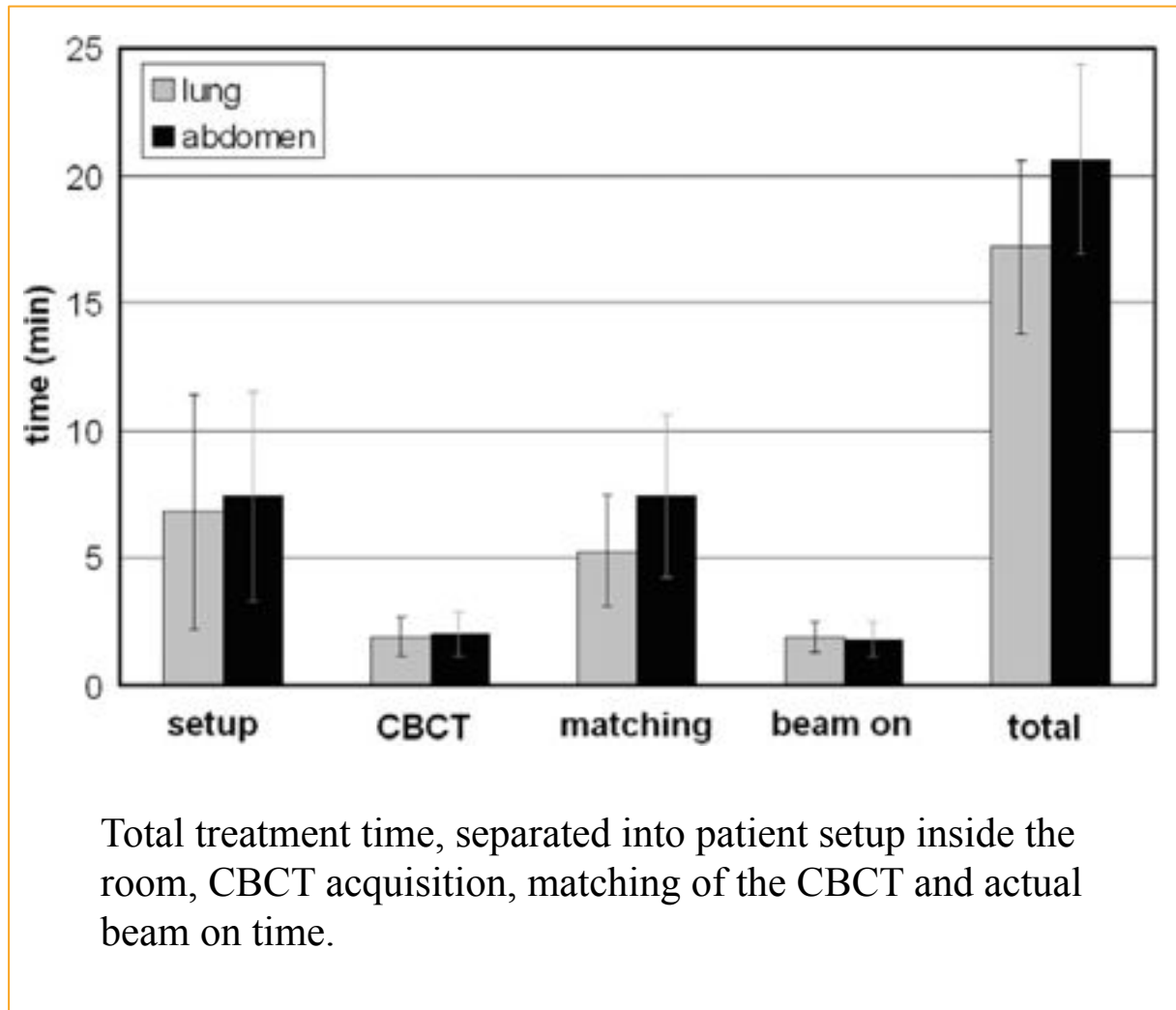
Purpose: To investigate the clinical application of FFF beams at maximum dose rate for SBRT.

Methods and materials: Patients with tumors in the lung or abdomen were subjected to SBRT using 6 MV FFF or 10 MV FFF beams. For each patient, three plans were calculated using 6 MV flattened, 6 MV FFF, and 10 MV FFF beams. Treatment times were recorded and analyzed, and tumor displacements were assessed by pre- and post-treatment cone beam computed tomography (CBCT).

Clinical Applications

Results: Altogether, 26 patients (16 lung, 10 abdominal tumors) were treated.

The average dose rate per patient ranged from 442 to 1860 MU/min. Beam-on time was on average 1.6 min (1SD = 0.6 min), with the total treatment times recorded at 18.5 min (1SD = 3.5 min). **The time advantage of using FFF beams was dose-dependent and started at 4 Gy for 6 MV FFF and at 10 Gy for 10 MV FFF beams.**



Clinical Applications



Flattening filter-free linac improves treatment delivery efficiency in stereotactic body radiation therapy

Brendan M. Prendergast,¹ John B. Fiveash,^{1a} Richard A. Popple,¹ Grant M. Clark,¹ Evan M. Thomas,¹ Douglas J. Minnich,² Rojymon Jacob,¹ Sharon A. Spencer,¹ James A. Bonner,¹ Michael C. Dobelbower¹

A total of 111 lung and liver SBRT cases treated from July 2008 to July 2011 were reviewed and 99 cases with complete data were identified.

Treatment delivery times for cases treated with a **FFF linac versus a conventional dose rate linac were compared**. The frequency and type of intrafraction image guidance was also collected and compared between groups.

In the FFF cohort, the mean treatment time and patient's immobilization was 11.44 (± 6.3) and 21.08 (± 6.8) minutes compared to 32.94 (± 14.8) and 47.05 (± 17.6) minutes for the conventional cohort ($p < 0.01$ for all values).

For lung and liver SBRT, a FFF linac reduces treatment and immobilization time by more than 50% compared to a conventional linac.

Clinical Applications



Fast Arc Delivery for Stereotactic Body Radiotherapy of Vertebral and Lung Tumors

Chin Loon Ong, M.Sc., Wilko F.A.R. Verbakel, Ph.D., Max Dahele, M.B.Ch.B., M.Sc., F.R.C.R., F.R.C.P., Johan P. Cuijpers, Ph.D., Ben J. Slotman, M.D., Ph.D., and Suresh Senan, Ph.D., M.R.C.P., F.R.C.R.

Methods and Material: Ten patients with peripheral lung tumors and 10 with vertebral metastases were planned using RapidArc with a flattened 6-MV photon beam and a 10-MV FFF beam for fraction doses of 7.5e18 Gy.

Results: **No major dosimetric differences** were seen between the two delivery techniques.

For **lung SBRT plans, conformity indices and OAR doses were similar**, although the average MU required were higher with FFF plans.

For **vertebral SBRT**, FFF plans provided **comparable PTV coverage, with no significant differences in OAR doses**. Average beam **delivery times were reduced** by a factor of up to 2.5, with all FFF fractions deliverable within 4 min.

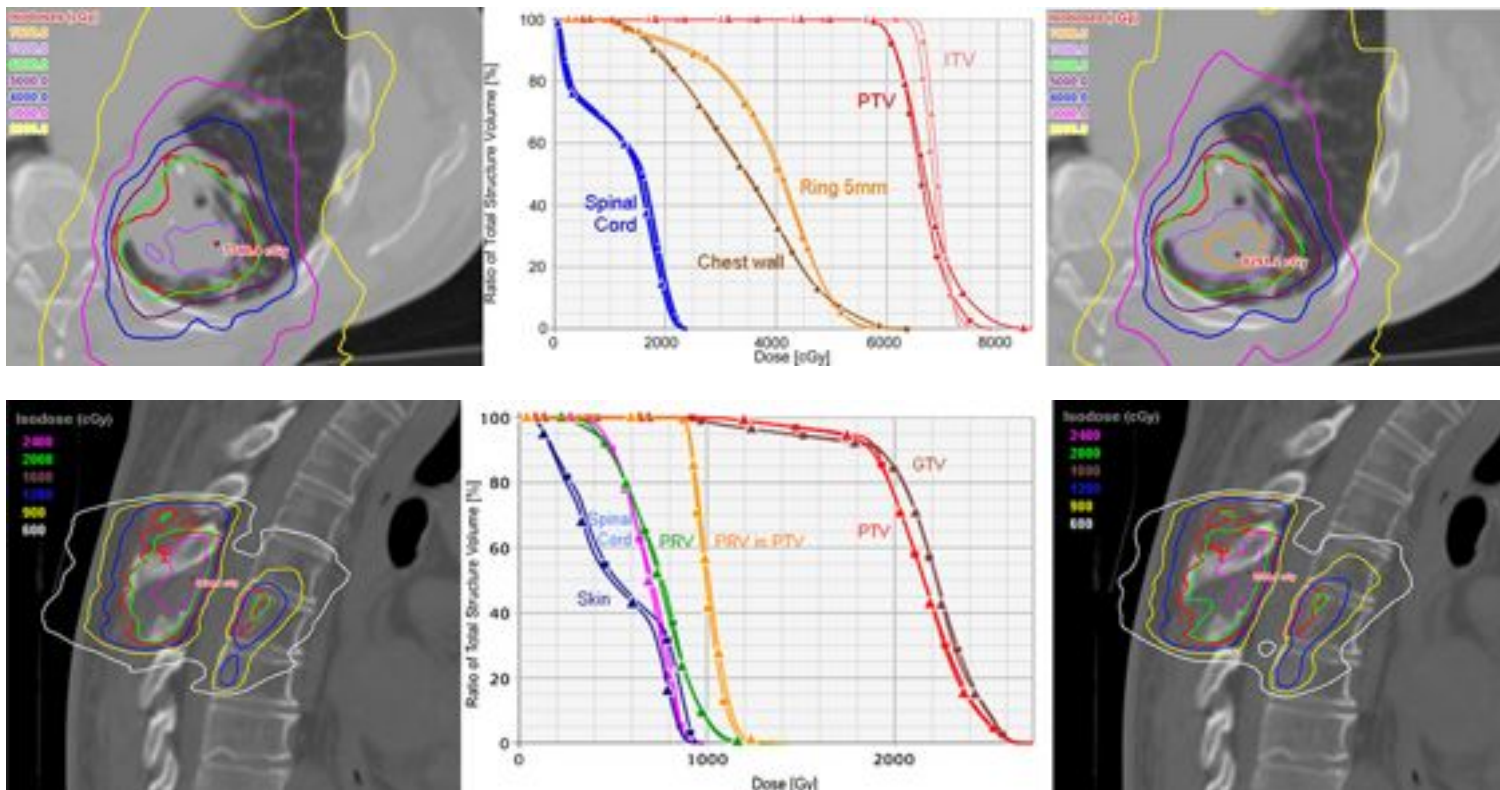
Conclusion: The **higher dose rate of FFF RapidArc reduces delivery times significantly, without compromising plan quality or accuracy of dose delivery**.

Clinical Applications



Fast Arc Delivery for Stereotactic Body Radiotherapy of Vertebral and Lung Tumors

Chin Loon Ong, M.Sc., Wilko F.A.R. Verbakel, Ph.D., Max Dahele, M.B.Ch.B., M.Sc., F.R.C.R., F.R.C.P., Johan P. Cuijpers, Ph.D., Ben J. Slotman, M.D., Ph.D., and Suresh Senan, Ph.D., M.R.C.P., F.R.C.R.



Comparison of dose distributions in sagittal planes for lung and vertebral flattened beam plan (left) and flattening filter free plan (right), with planning target volume outlined in red. The DVH shows similar target coverage and organ at risk sparing between 6-MV flattened beam plan (squares) and 10-MV FFF (triangles).

Clinical Applications



Feasibility and early clinical assessment of flattening filter free (FFF) based stereotactic body radiotherapy (SBRT) treatments

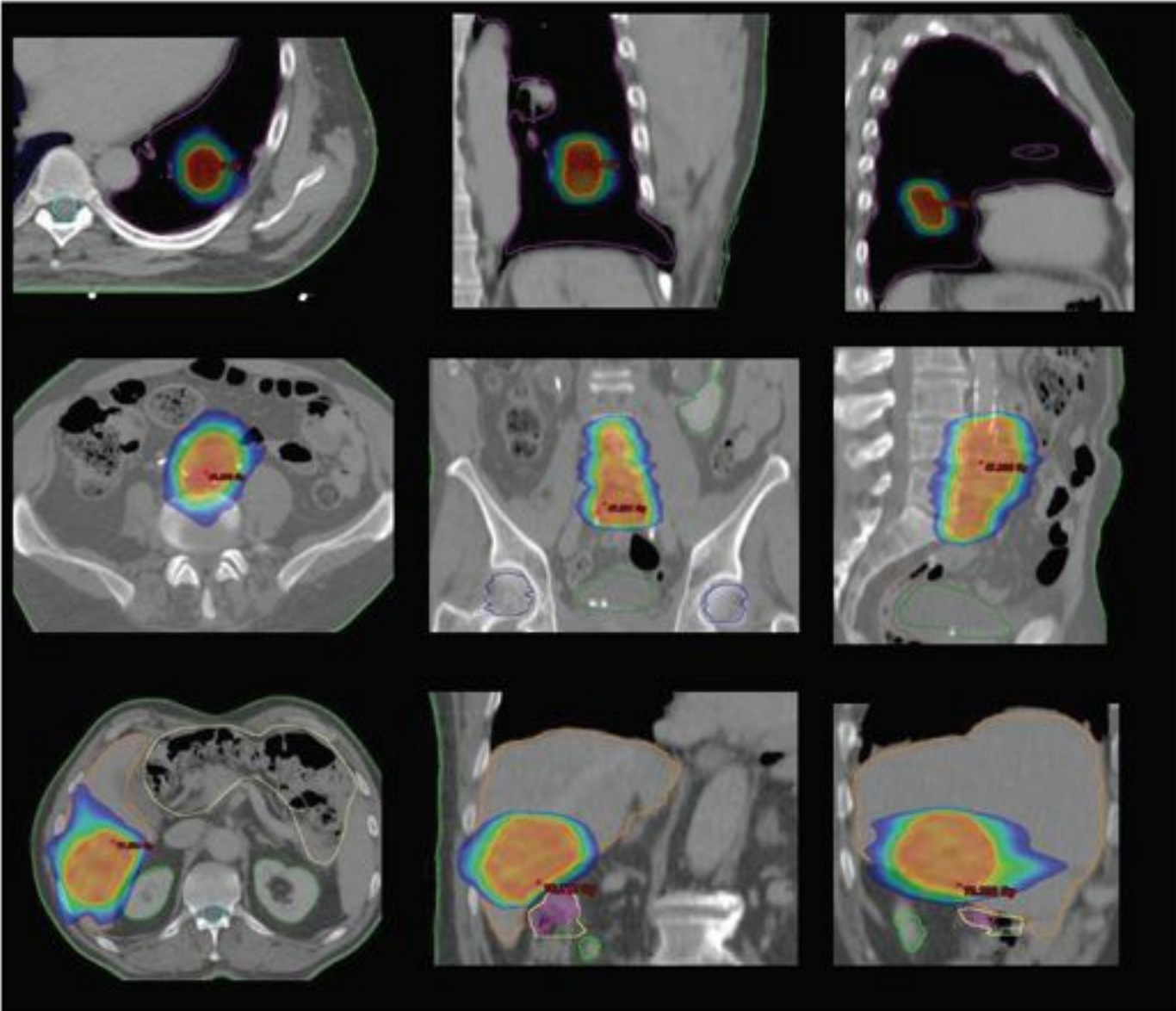
Marta Scorsetti¹, Filippo Alongi^{1*}, Simona Castiglioni¹, Alessandro Clivio², Antonella Fogliata², Francesca Lobefalo¹, Pietro Mancosu¹, Pierina Navarria¹, Valentina Palumbo¹, Chiara Pellegrini¹, Sara Pentimalli¹, Giacomo Reggiori¹, Anna M Ascolese¹, Antonella Roggio¹, Stefano Arcangeli¹, Angelo Tozzi¹, Eugenio Vanetti² and Luca Cozzi²

Purpose: To test feasibility and safety of clinical usage of Flattening Filter Free (FFF) beams for delivering SBRT doses to various tumor sites, by means of Varian TrueBeam™ (Varian Medical Systems).

Methods and Materials: **70 patients were treated with SBRT and FFF:** 51 lesions were in the thorax (48 patients), 10 in the liver, 9 in isolated abdominal lymph node, adrenal gland or pancreas.

Lung lesions were treated with cumulative doses of 32 or 48 Gy, delivered in 4 consecutive fractions. The liver patients were treated in 3 fractions with total dose of 75 Gy. The isolated lymph nodes were irradiated in 6 fractions with doses of 45 Gy.

Clinical Applications



Examples of dose distributions for the three groups of patients.

Colour wash scale is from 20 to 50 Gy for the lung and the abdominal cases and from 35 to 80 Gy for the liver case.

Results: The minimum follow-up was 3 months.

Six cases of acute toxicities were recorded (2 Grade2 and 2 Grade3 in lung and 2 Grade2 in abdomen).

No patient experienced acute toxicity greater than Grade3.

Clinical Applications: Brain



Intensity modulated radiosurgery of brain metastases with flattening filter-free beams

Florian Stieler^{*}, Jens Fleckenstein, Anna Simeonova, Frederik Wenz, Frank Lohr

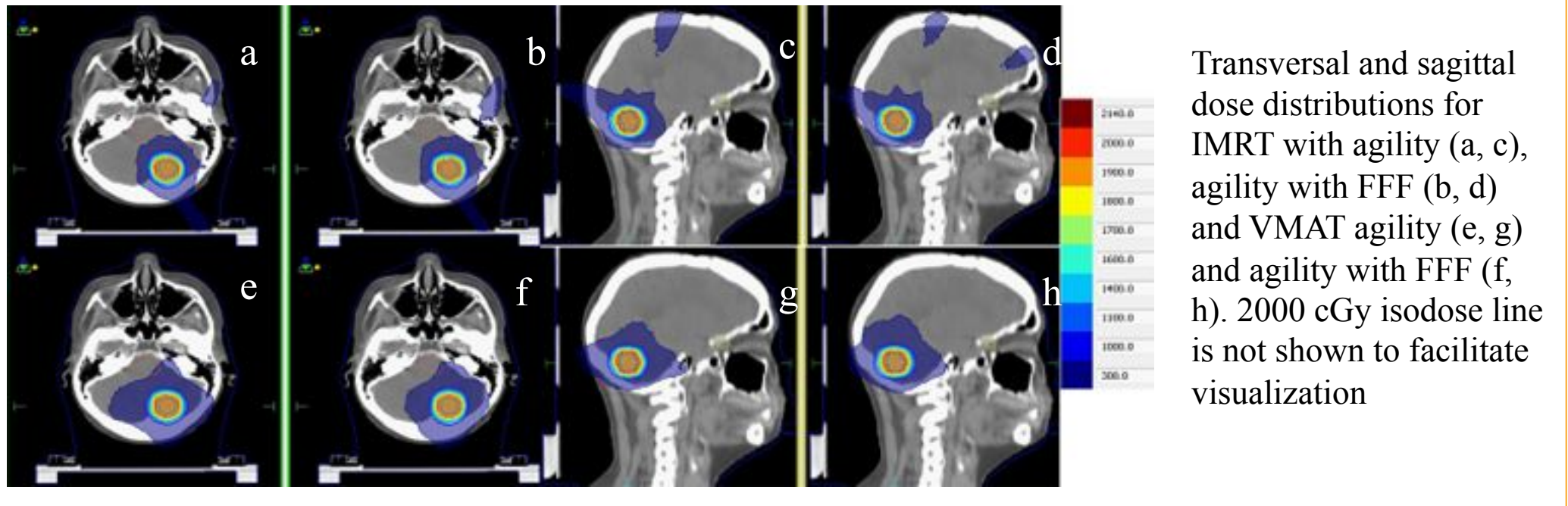
Department of Radiation Oncology, University Medical Center Mannheim, University of Heidelberg, Germany

Material and Methods: CT data of 15 patients with brain metastases were included in this study. For every patient, **2 IMRT- and 2 VMAT-plans were created** using a high-resolution MLC with two different delivery modes (**6 MV standard vs. 6 MV FFF**).

Plan quality and efficiency was assessed by analysis of **conformity, homogeneity, dose gradients, treatment delivery time and number of monitor units (MU)**.

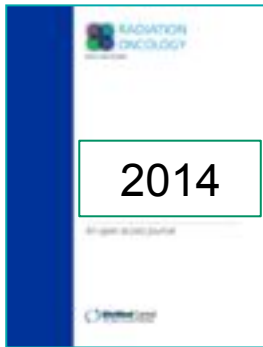
Results: Plan quality was similar for both approaches. **FFF provided a mean treatment time reduction of 51.5% with similar MU for VMAT and IMRT** for this low-modulation paradigm.

Clinical Applications: Brain



Conclusion: **FFF radiosurgery is an efficient technique** for intensity modulated hypofractionated or single fraction treatments with **similar plan quality** when compared to flattened beams at **reduced treatment time**.

Clinical Applications: Brain



Critical appraisal of RapidArc radiosurgery with flattening filter free photon beams for benign brain lesions in comparison to GammaKnife: a treatment planning study

Ufuk Abacioglu¹, Zeynep Ozen¹, Meltem Yilmaz², Alptekin Arifoglu¹, Basri Gunhan¹, Namik Kayalilar¹, Selcuk Peker², Meric Sengoz², Salih Gurdalli¹ and Luca Cozzi^{3*}

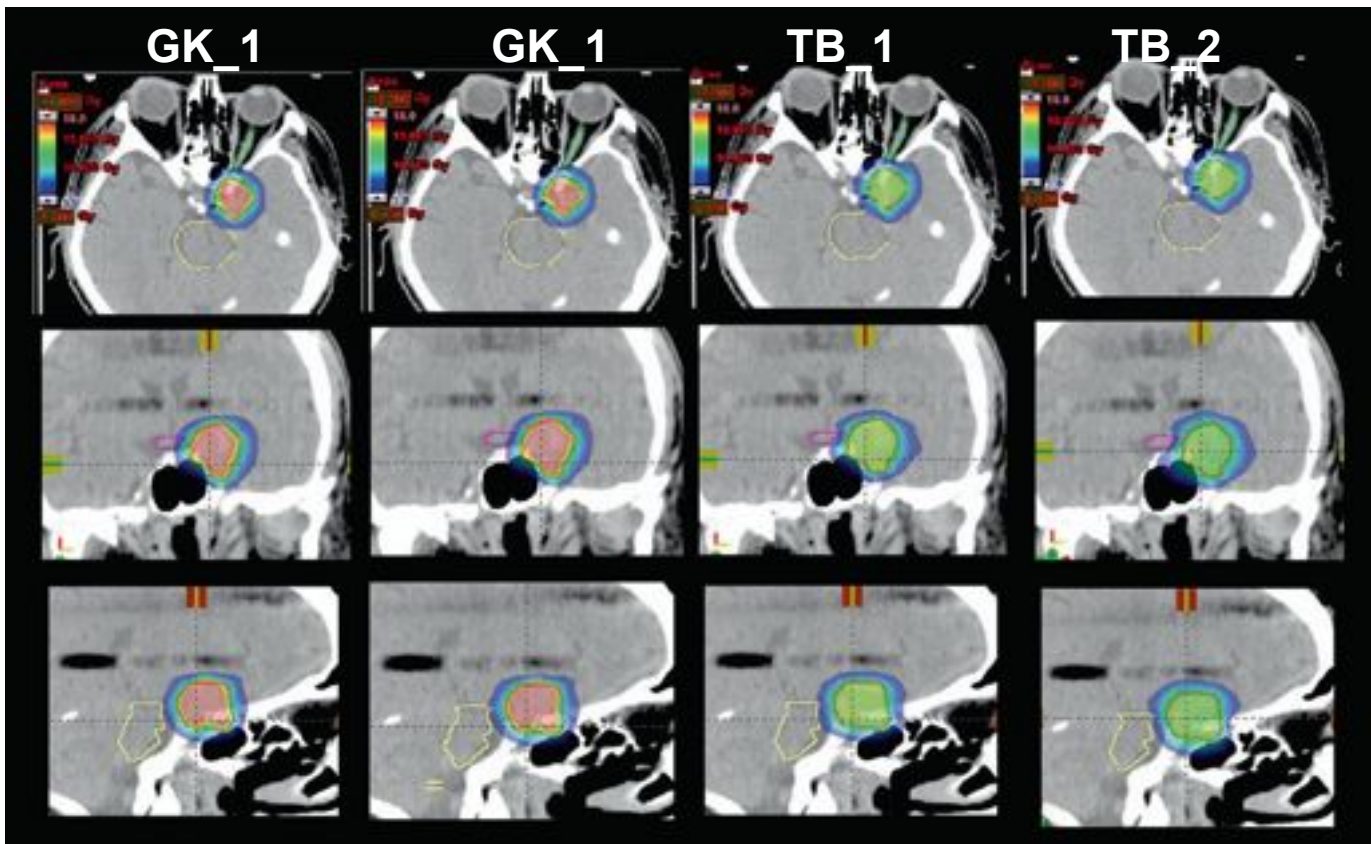
Methods: Twelve patients with **vestibular schwannoma** (VS, n = 6) or **cavernous sinus meningioma** (CSM, n = 6) were planned for both **SRS using volumetric modulated arc therapy (VMAT)** by RA. 104 MV **flattening filter free** photon beams with a maximum dose rate of 2400 MU/min were selected. Data were compared **against plans optimised for GK**.

A **single dose of 12.5 Gy** was prescribed.

The primary objective was to assess **treatment plan quality**.

Secondary aim was to appraise **treatment efficiency**.

Clinical Applications: Brain



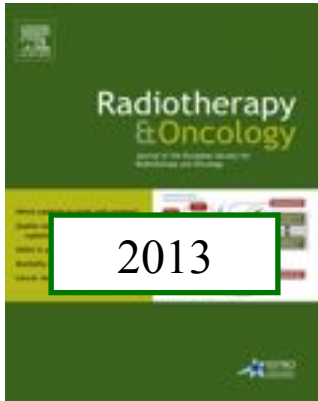
The isodose distribution for the four plans in axial, coronal and sagittal planes for a representative Meningioma case. Color wash threshold is set between 5 and 18 Gy

Conclusions: SRS with RA and FFF beams revealed to be **adequate and comparable to GK** in terms of target coverage, homogeneity, organs at risk sparing with **some gain in terms of treatment efficiency.**

Clinical Applications: Lung

Authors	N. pts	T or M	N. Of lesions	Total dose/frs	LC	Toxicity
Navarria 2013	46	T1-T2	46	48Gy/4fr	100% (1y.)	G1-2 17% G3 4%
Prendergast 2013	64	T1-T2	64	48Gy/4fr (range: 30–60 Gy / 3–5 frs)	Not reported	≤ 90 days: G2 8% G3 2% >90 days: G2 12% G3 6% G4 1% G5 1%
Navarria 2014	76	M	118	48Gy/4fr 60Gy/3fr 60Gy/8fr	95% (1y.) 89% (2ys.) 89% (3ys.)	No acute toxicity occurred

Clinical Applications: Lung

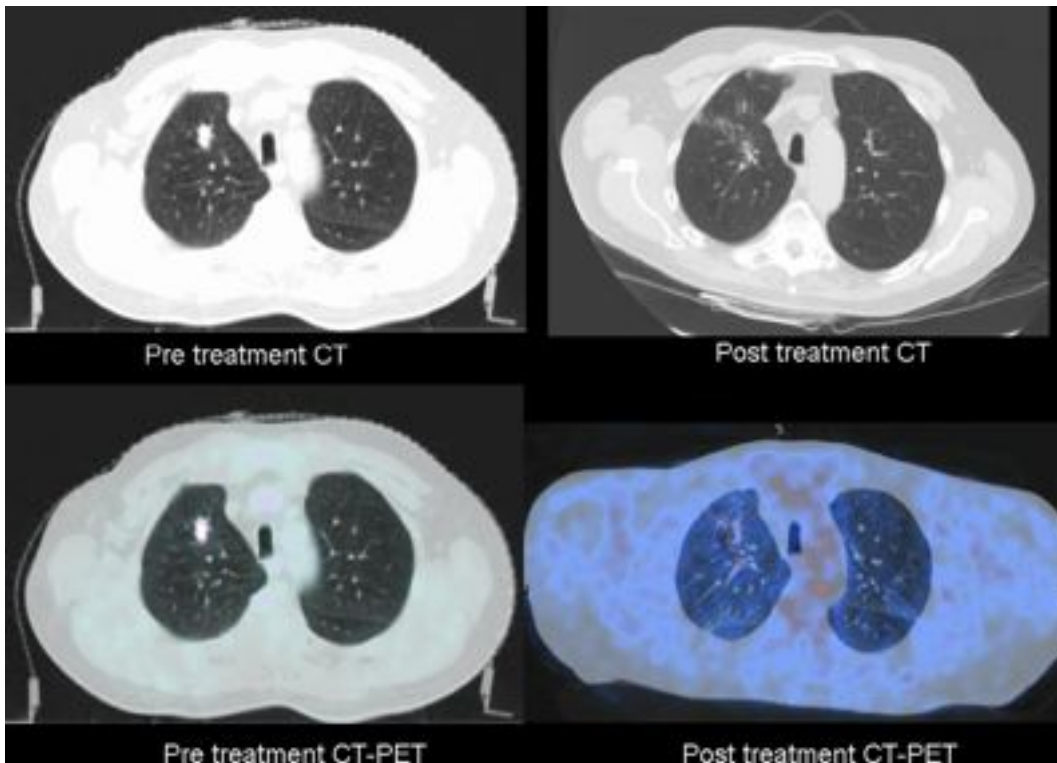


SBRT of lung cancer

Volumetric modulated arc therapy with flattening filter free (FFF) beams for stereotactic body radiation therapy (SBRT) in patients with medically inoperable early stage non small cell lung cancer (NSCLC)

Pierina Navarria^{a,*}, Anna Maria Ascolese^a, Pietro Mancosu^a, Filippo Alongi^a, Elena Clerici^a, Angelo Tozzi^a, Cristina Iftode^a, Giacomo Reggiori^a, Stefano Tomatis^a, Maurizio Infante^b, Marco Alloisio^b, Alberto Testori^b, Antonella Fogliata^c, Luca Cozzi^c, Emanuela Morengi^a, Marta Scorsetti^a

^a Radiotherapy and Radiosurgery Department; ^b Department of Thoracic Surgery, Humanitas Cancer Center, Istituto Clinico Humanitas, Milan, Italy; ^c Oncology Institute of Southern Switzerland, IOSI, Bellinzona, Switzerland



CT and CT-PET scan performed before (left) and after (right) treatment. A complete remission can be seen.

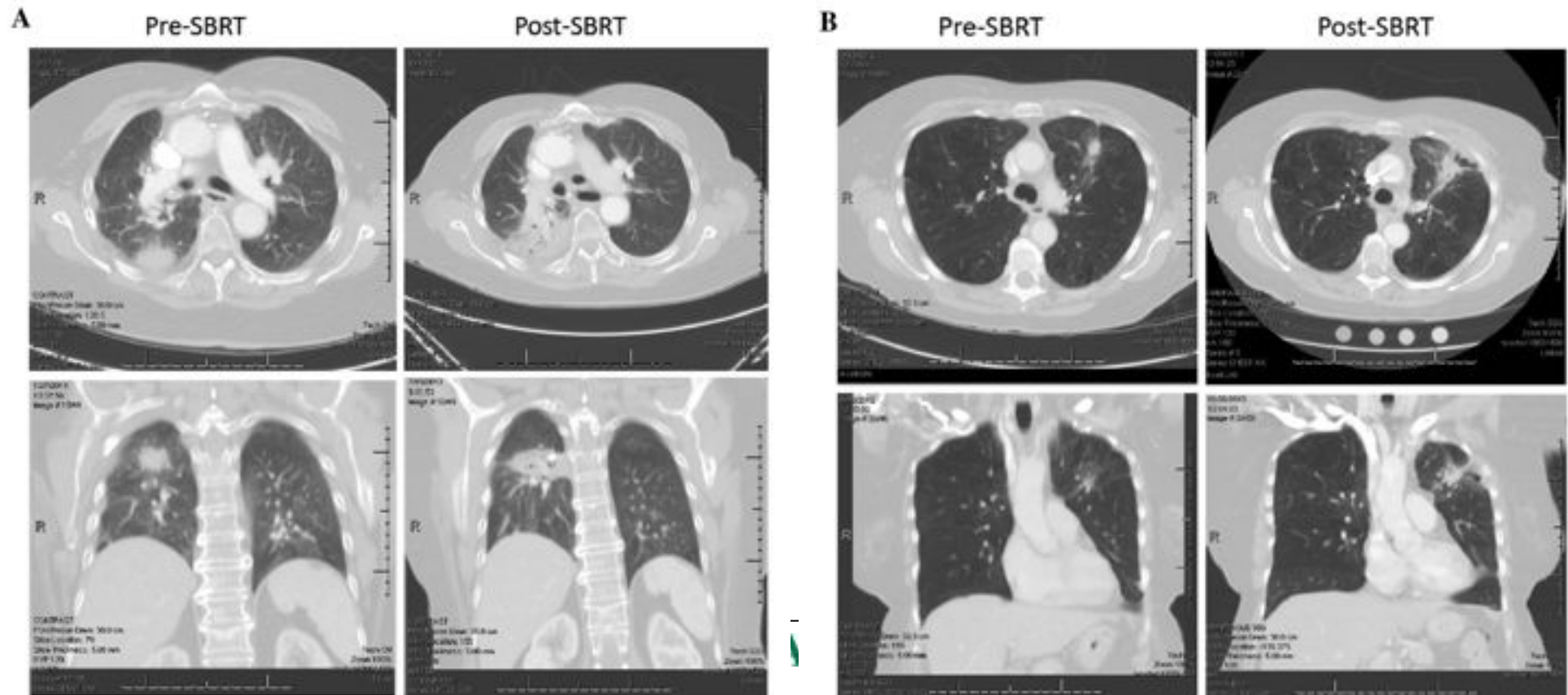
Clinical Applications: Lung

RADIATION ONCOLOGY

2013

Stereotactic body radiation therapy (SBRT) for lung malignancies: preliminary toxicity results using a flattening filter-free linear accelerator operating at 2400 monitor units per minute

Brendan M Prendergast^{1*}, Michael C Dobelbower², James A Bonner², Richard A Popple², Craig J Baden², Douglas J Minnich³, Robert J Cerfolio³, Sharon A Spencer² and John B Fiveash²



Clinical Applications: Lung



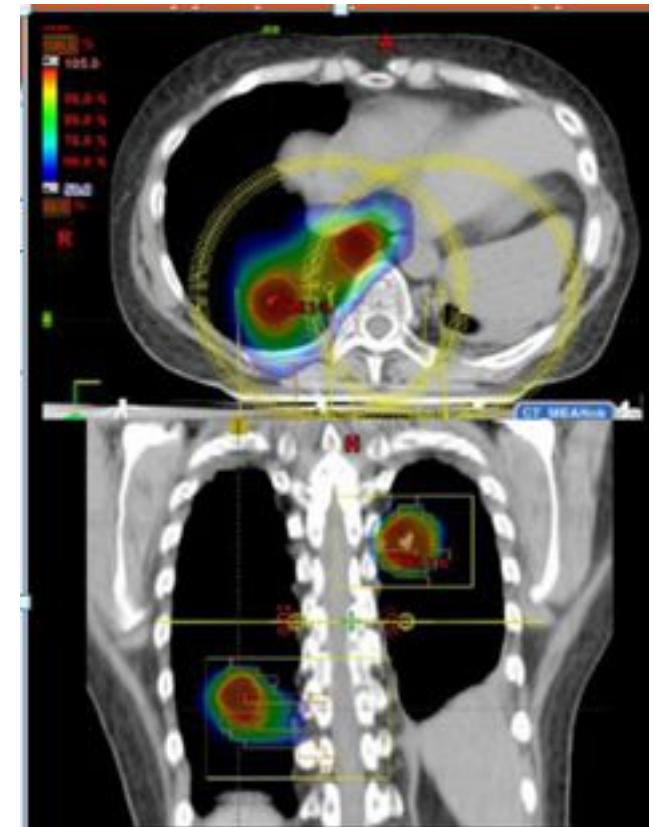
Stereotactic body radiotherapy (sbirt) in lung oligometastatic patients: role of local treatments

Pierina Navarria^{1*}, Anna Maria Ascolese¹, Stefano Tomatis¹, Luca Cozzi², Fiorenza De Rose¹, Pietro Mancosu¹, Filippo Alongi¹, Elena Clerici¹, Francesca Lobefalo¹, Angelo Tozzi¹, Giacomo Reggiori¹, Antonella Fogliata² and Marta Scorsetti¹

From October 2010 to February 2012, 76 consecutive patients for 118 lung lesions were treated.

The local control at 1, 2 and 3 years was 95%, 89% and 89% respectively. No major pulmonary toxicity, chest pain or rib fracture occurred. The median follow up was 20 months (range 6–45 months). Overall Survival (OS) at 1, 2 and 3 years was 84.1%, 73% and 73% respectively.

Conclusions: SABR is feasible with limited morbidity and promising results in terms of local control, survival and toxicity.



Clinical Applications: Lung

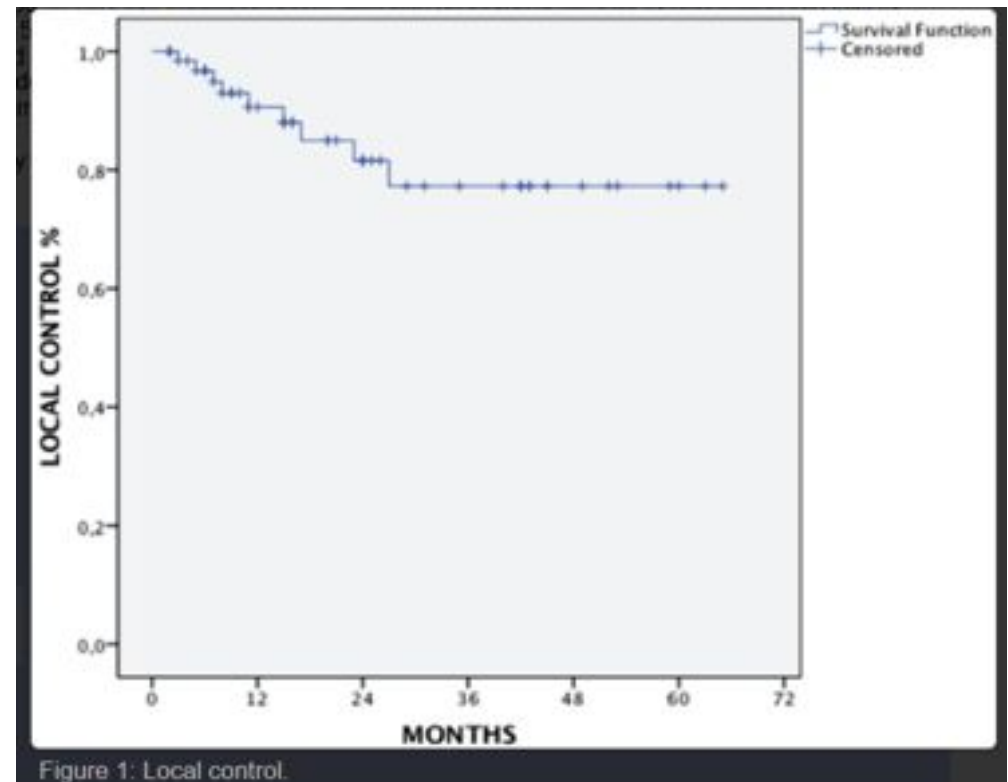
Technol Cancer Res Treat. 2014 Feb;13(1):37-45. doi: 10.7785/tcr.2012.500355. Epub 2013 Jun 24.

Outcomes of single fraction stereotactic ablative radiotherapy for lung metastases.

Filippi AR¹, Badellino S, Guarneri A, Levis M, Botticella A, Mantovani C, Ragona R, Racca P, Buffoni L, Novello S, Ricardi U.

102 patients treated with SABR, a **single dose of 26 Gy prescribed to the 80% isodose**, by 3D-CRT or by IGRT-VMAT.

These results might provide **supportive evidence to the use of single fraction SABR as a valid and acceptable alternative to surgery** for pulmonary metastases from different primary tumors



Clinical Applications: Prostate and Lymphnode

Site of disease	Authors	N. pts	T or M	N. Of lesions	Total dose/frs	LC	Toxicity
Prostate	Alongi et al. 2013	40	T	40	35 Gy / 5 fx	-	G1-2 60% G3-4 0%
Prostate	Zwahlen et al. 2011	7	T	7	57 Gy / 9 fx	-	-
Abdominal / pelvic lymphnodes	Alongi et al. 2012	25	M	28	45 Gy / 6 fx	100% (195 dd)	G1-2 14% G3-4 0%

Clinical Applications: Prostate



The Use of Photon Beams of a Flattening Filter-free Linear Accelerator for Hypofractionated Volumetric Modulated Arc Therapy in Localized Prostate Cancer

Daniel R. Zwahlen, M.D., Stephanie Lang, M.Sc., Jan Hrbacek, M.Sc., Christoph Glanzmann, M.D., Stephan Kloeck, Ph.D., Yousef Najafi, M.D., Tino Streller, Ph.D., Gabriela Studer, M.D., Kathrin Zaugg, M.D., Ph.D., and Urs M. Luetolf, M.D.

Methods and Materials: VMAT treatment planning was performed for 7 patients using TrueBeam linear accelerator and photon beams with (X6, X10) and without (X6FFF, X10FFF) flattening filter. Prescribed dose was $19 \times 3 \text{ Gy} = 57 \text{ Gy}$.

Results: No difference was detected between the four beams in PTV coverage, conformity, and homogeneity. X6FFF delivered 3.6% more dose compared with the X6 ($p < 0.01$). X10FFF delivered 3.0% ($p < 0.01$), and the X10 5.8% ($p < 0.01$) less mean body dose compared with X6. There was a significant increase in the mean dose to the rectum for the X10 compared with X6 (2.6%, $p < 0.01$).

Conclusion: FFF beams resulted in dose distributions similar to flattened beams. **X10FFF beam provided the best solution, sparing rectum and bladder and minimizing whole-body dose.** FFF beams lead to a **time efficient treatment delivery**, particularly when combined with hypofractionated VMAT.

Clinical Applications: Prostate



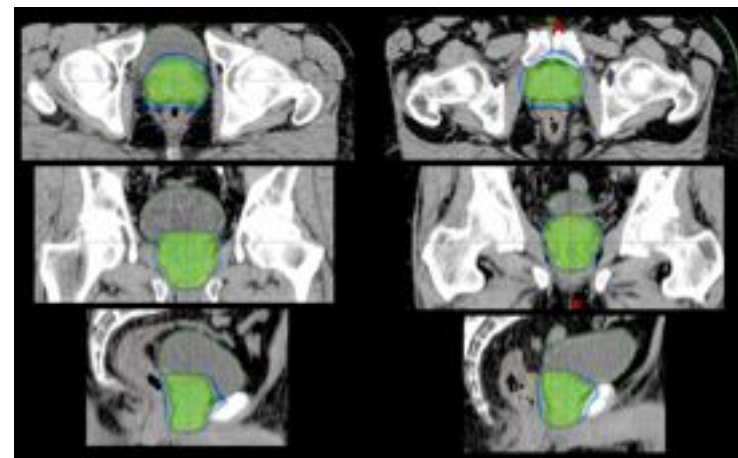
Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study

Filippo Alongi^{1,4*}, Luca Cozzi², Stefano Arcangeli¹, Cristina Iftode¹, Tiziana Comito¹, Elisa Villa¹, Francesca Lobefalo¹, Pierina Navarria¹, Giacomo Reggiori¹, Pietro Mancosu¹, Elena Clerici¹, Antonella Fogliata², Stefano Tomatis¹, Gianluigi Taverna³, Pierpaolo Graziotti³ and Marta Scorsetti¹

Prospective phase I-II study, started on February 2012.

The schedule was **35 Gy in 5 alternative days**.

Median follow-up was 11 months (range: 5–16); 40 patients were recruited in the protocol and treated.



Conclusions: Early findings suggest that SBRT with RapidArc and FFF beams for prostate cancer in 5 fractions **is feasible and tolerated in acute setting**.

Longer follow-up is needed for assessment of late toxicity and outcome.

Clinical Applications: Retreatment

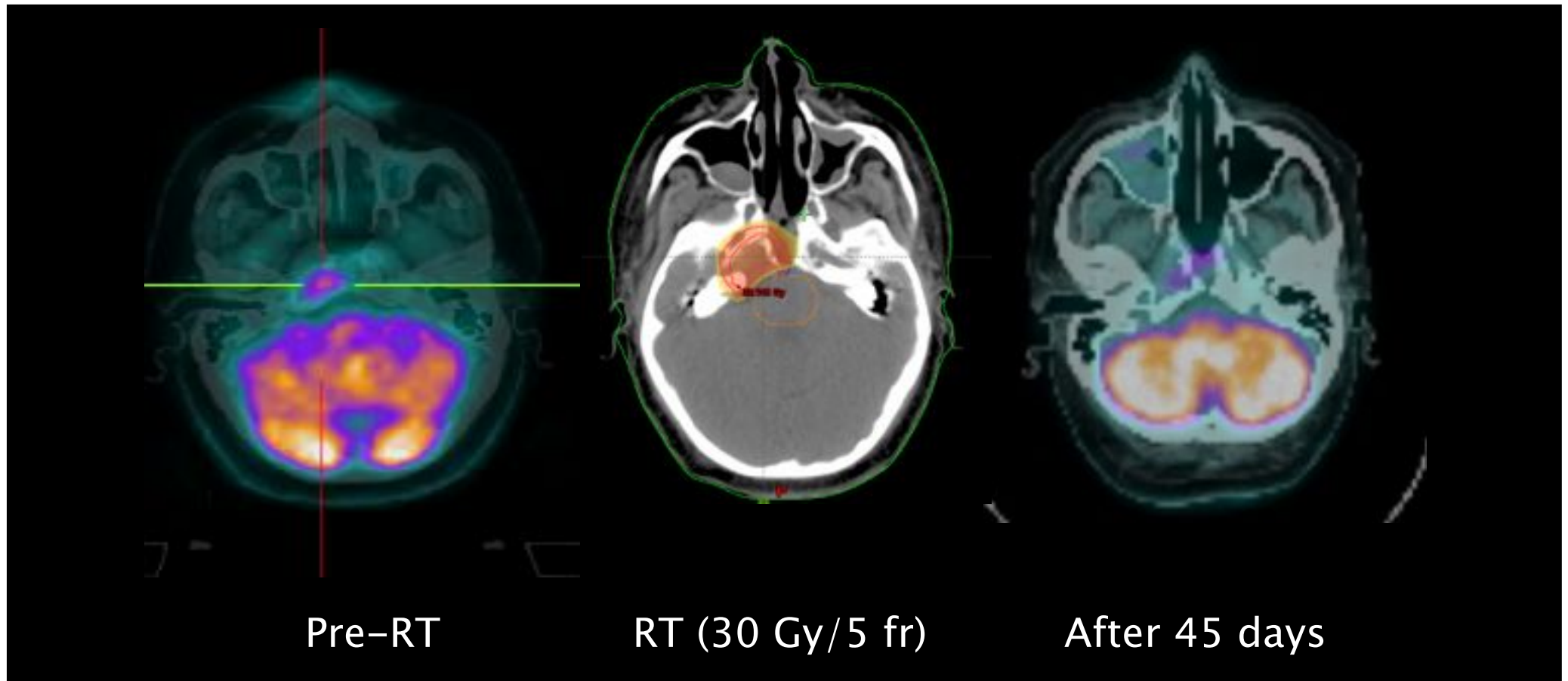
Site of disease	Authors	N. pts	T or M	N. Of lesions	Total dose/ frs	LC	Toxicity
Head-neck	Alongi et al. 2012	4	T	4	30 Gy / 5 fx 45 Gy / 18 fx	-	-
Vertebral	Ong et al. 2013	9	M	9	16 Gy / 1 fx 20 Gy / 2 fx 27 Gy / 3 fx	-	-

Clinical Applications: Retreatment



Initial experience of hypofractionated radiation retreatment with true beam and flattening filter free beam in selected case reports of recurrent nasopharyngeal carcinoma

Filippo Alongi*, Elena Clerici, Sara Pentimalli, Pietro Mancosu, Marta Scorsetti



Clinical Applications: Abdomen

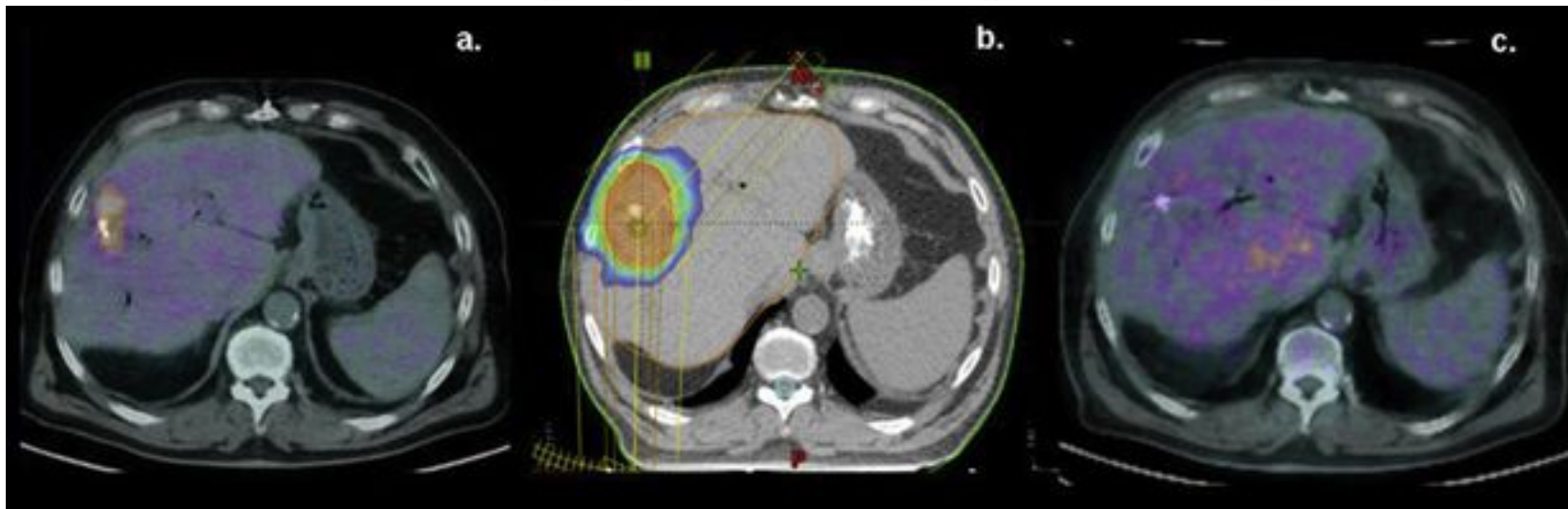
Site of disease	Authors	N. pts	T or M	N. Of lesions	Total dose/frs	LC	Toxicity
Liver	Lang et al. 2013	4	-	4	50 Gy / 5 fx 40 Gy / 4 fx 48 Gy / 4 fx	-	-
Liver	Wang et al. 2014	20	T	22	50 Gy / 10 fx	-	G1-2 25% G3-4 5%
Liver	Scorsetti et al. 2013	61	M	76	75Gy/3fr	94% (1y.)	G2 26% None of the patients experienced G3 or higher acute toxicity
Pancreas	Lang et al. 2013	4	-	4	12 Gy / 2 fx 50 Gy / 10 fx	-	-
Pancreas	Tozzi et al.	30	T or recurrence	30	45Gy/6fr	FFLP 96% at 1 and 2 ys.	G1 26% G2 10%
Adrenal gland	Lang et al. 2013	2	-	2	30 Gy / 3 fx 40 Gy / 4 fx	-	-

Clinical Applications: Liver



Is Stereotactic Body Radiation Therapy an Attractive Option for Unresectable Liver Metastases? A Preliminary Report From a Phase 2 Trial

Marta Scorsetti, MD,* Stefano Arcangeli, MD,* Angelo Tozzi, MD,* Tiziana Comito, MD,* Filippo Alongi, MD,* Pierina Navarria, MD,* Pietro Mancosu, MSc,* Giacomo Reggiori, MSc,* Antonella Fogliata, MSc,† Guido Torzilli, MD,† Stefano Tomatis, MSc,* and Luca Cozzi, PhD†



Patient treated with stereotactic body radiation therapy for recurrence of liver metastasis after surgery.

Conclusions: SBRT for unresectable liver metastases can be considered an **effective, safe, and noninvasive therapeutic option**, with **excellent rates of local control** and a **low treatment-related toxicity**

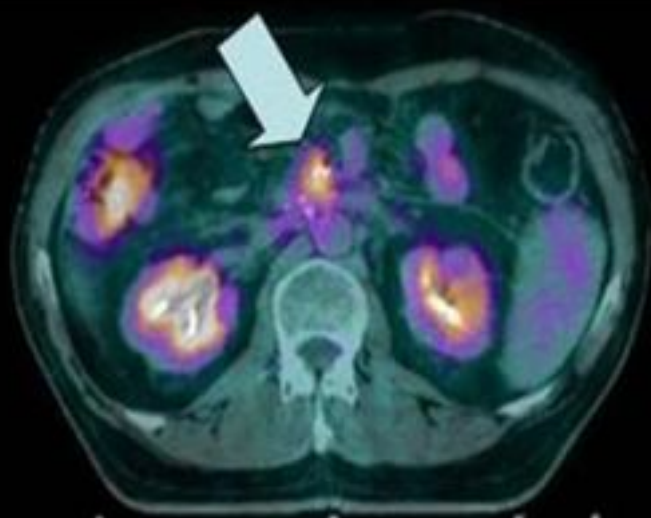
Clinical Applications: Pancreas

RADIATION ONCOLOGY

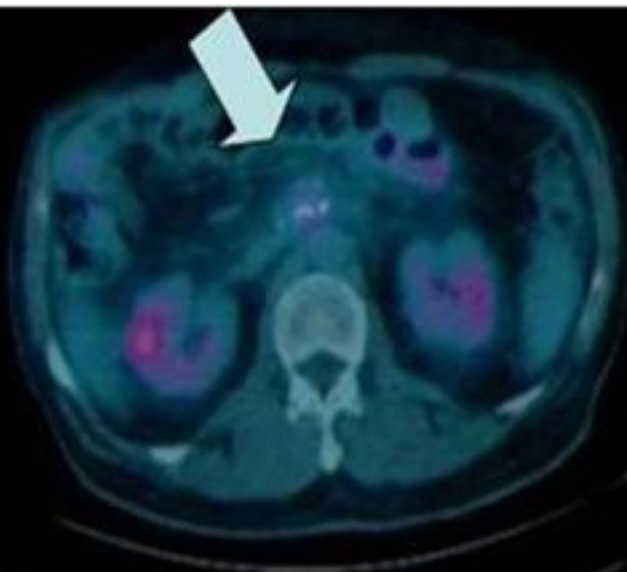
2013

SBRT in unresectable advanced pancreatic cancer: preliminary results of a mono-institutional experience

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Pre-RT PET/CT



Complete Response
after 6 months

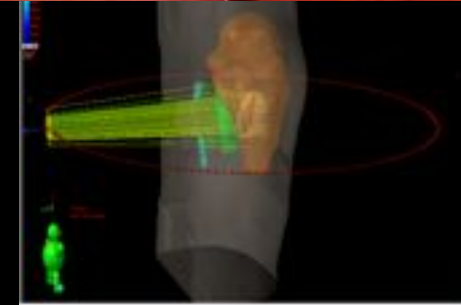
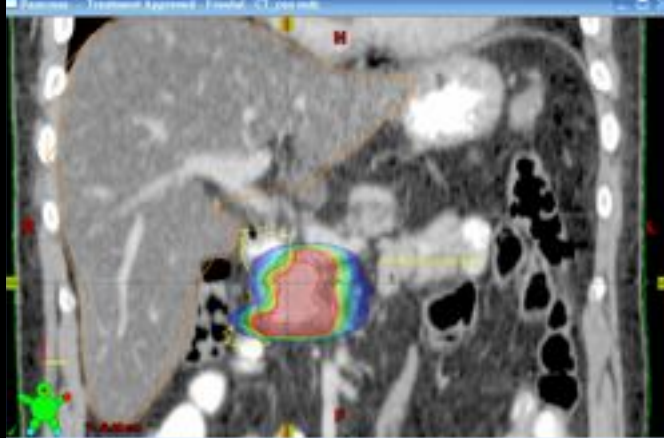
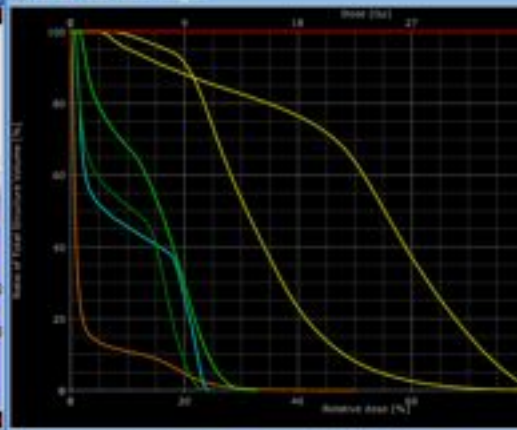
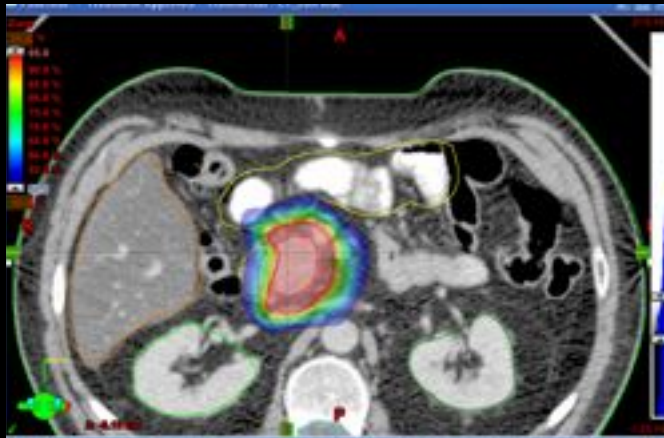
Conclusions:

Our preliminary results show that SBRT can obtain a **satisfactory local control rate** for unresectable locally advanced and recurrent pancreatic adenocarcinoma.

This fractionation schedule is **feasible**, and **no G \geq 3 toxicity was observed**.

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Pz 56 y. Pancreatic adenoca unresectable;
GEM + FOLFIRI -> RP -> SBRT (45Gy/6fr.) -> surgery (R0).



Conclusions

1. Planning studies demonstrate **potential benefit for dose distributions**
2. Early clinical data focused on **LC** and **acute toxicity** demonstrate **good impact** on several primary indications
3. **Late results on OS and toxicity are maturing** but so far no unexpected findings.
4. **Motion management**: faster delivery directly impacts on better control of OAR motion and patient compliance
5. **Non conventional fractionation, retreatments, SABR, radiosurgery** in more areas are practically doable with FFF opening more clinical applications
6. **Cost effectiveness**: capital cost slightly higher, running costs equivalent, throughput increased

Thanks



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