

Can external beam radiotherapy replace interventional radiotherapy?



Andrea Vavassori

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RAO Radioterapia e Oncologia clinica

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Radioterapia di precisione per un'oncologia innovativa e sostenibile

DICHIARAZIONE

Relatore: Andrea Vavassori

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Consulenza ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazione ad Advisory Board (NIENTE DA DICHIARARE)
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Altro



KEEP

NO CONFLICT



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Radioterapia di precisione per un'oncologia innovativa e sostenibile

Han. Trends in the utilization of BT in cervical cancer in the United States. IJROB 2013

Gill. National Cancer Data Base analysis of RT consolidation modality for cervical cancer: the impact of new technological advancements IJROB 2014

Eifel. Patterns of RT practice for patients treated for intact cervical cancer in 2005 to 2007: a quality research in radiation oncology study IJROB 2014

- SEER (Surveillance Epidemiology and End Results)
- NCDB (National Cancer Data Base)
- Quality Research in Radiation Therapy





Radioterapia di precisione per un'oncologia innovativa e sostenibile



A national survey of AIRO (Italian Association of Radiation Oncology) brachytherapy (Interventional Radiotherapy) study group

Rosa Autorino, MD, PhD¹, Lisa Vicenzi, MD², Luca Tagliaferri, MD, PhD¹, Carlo Soatti, MD³, Prof. Gyeorgy Kovacs, MD, PhD⁴, Cynthia Aristei, MD⁵ J Contemp Brachytherapy 2018, 10, 3: 254–259

>50% of centres did not deliver IRT treatments because of lack of skilled personnel



Lack of personel (47%)
Lack of expertise (11%)
Need to update equipment (5%)
CPSTS/TIME consuming (7%)
Not specified (30%)





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Some patients cannot be treated by IRT:

- tumor dimensions and/or locations
- anatomical variations
- risk of bleeding
- medical comorbidities that preclude anesthesia especially in the interstitial procedures
- patient's refusal due to anxiety or discomfort













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CrossMark



IMRT vs HDR-BT

APBI: 7 x 4.3 Gy

Breast Cancer Treatment



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	Radiotherapy and Oncology 122 (2017) 17-23	
	Contents lists available at ScienceDirect	Radiotherapy
	Radiotherapy and Oncology	
ELSEVIER	journal homepage: www.thegreenjournal.com	40

Breast brachytherapy

Multicatheter interstitial brachytherapy versus intensity modulated external beam therapy for accelerated partial breast irradiation: A comparative treatment planning study with respect to dosimetry of organs at risk

Tibor Major*, Gábor Stelczer, Csilla Pesznyák, Norbert Mészáros, Csaba Polgár

The target volume can be appropriately irradiated by both techniques, but MIBT spares OAR better than IMRT

Multicatheter interstitial brachytherapy versus stereotactic radiotherapy with CyberKnife for accelerated partial breast irradiation: a comparative treatment planning study with respect to dosimetry of organs at risk

András Herein^{1,2}, Gábor Stelczer^{1,2}, Csilla Pesznyák^{1,2}, Georgina Fröhlich^{1,3}. Viktor Smanykó¹, Norbert Mészáros^{1,4}, Csaba Polgár^{1,4}, Tibor Major^{1,4} _{Radiol Oncol 2021; 55(2): 229-239.} CK vs HDR-BT

• APBI: 4 x 6.25 Gy



The target can be properly irradiated by both techniques with similar dose distributions and high dose conformity

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Prostate Cancer Treatment



Radioterapia di precisione per un'oncologia innovativa e sostenibile



planning for tomotherapy, cyberknife and VMAT Romena de Chavez, MSc^{1,8,*}, Garry Grogan, MSc¹, Ben Hug, MSc⁵, Kate Howe, BSc[‡],

Komena de Chavez, MSC^{***}, Garty Grogan, MSC^{*}, Ben Hug, MSC^{*}, Kate Howe, BSC^{*}, Alice Grigg, BSC[§], David Waterhouse, PhD^{1,#}, Jonathan Lane, MSC[†], Alan Glyde, BSC[‡], Elizabeth Brown, PhD[‡], Sean Bydder, BHB, MBChB, MBA, MPH, FRANZCR^{†,#}, David Pryor, BSC, MBBS, FRANZCR[‡], Cathy Hargrave^{‡,§}, Paul H. Charles, PhD^{1,§,**,††,1,2}, James Hellyer, MSC[#], Martin A. Ebert, PhD^{1,§,II}







CK



VMAT



HDR BT

TomoTherapy

SBRT cannot achieve the same high intraprostatic doses as HDR BT while respecting the OAR constraints

BUT...

Physician preference remains the most

significant factor in the nonutilization of IRT





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Skin Cancer Treatment



Strahlenther Onkol (2021) 197:547–554 https://doi.org/10.1007/s00066-021-01759-4

ORIGINAL ARTICLE

Dosimetric comparison of volumetric modulated arc therapy (VMAT) and high-dose-rate brachytherapy (HDR-BT) for superficial skin irradiation with significant curvature in one or more planes

Rachel J. Wills¹ · Gerry Lowe¹ · Caroline L. Jones² · Peter J. Hoskin^{1,3}

14 pts HDR-BT or VMAT (scalp and lower limbs)

Maximum skin surface dose: HDR-BT > VMAT

Volumes of OAR: VMAT < HDR-BT \rightarrow **TPS**?















Gynecologic Cancer Treatments



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Applied Radiation Oncology 2015

Non-brachytherapy alternatives in cervical cancer radiotherapy: Why not?

Sarah Kilic, BA, MA; Bernadette Cracchiolo, MD, MPH; Omar Mahmoud, MD, PhD



- Cervical cancer is the 3rd / 4th most common cancer
- IRT is the gold standard boost (improves OS & LC)





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10.712	Sei	264
2023	28	2
	161	81
1	100	عطانة

Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 4, pp. 1272–1278, 2008 Copyright © 2008 Elsevier Inc. Printed in the USA. All rights reserved 0360-30160K85-see from matter

doi:10.1016/j.ijrobp.2008.03.032

2008

PHYSICS CONTRIBUTION

IMAGE-GUIDED RADIOTHERAPY FOR CERVIX CANCER: HIGH-TECH EXTERNAL BEAM THERAPY VERSUS HIGH-TECH BRACHYTHERAPY

DIETMAR GEORG, PH.D., CHRISTIAN KIRISITS, PH.D., MARTIN HILLBRAND, M.SC., JOHANNES DIMOPOULOS, M.D., AND RICHARD PÖTTER, M.D., PH.D. Strahlenther Onkol (2022) 198:93–109 https://doi.org/10.1007/s00066-021-01867-1

REVIEW ARTICLE

The value of brachytherapy in the age of advanced external beam radiotherapy: a review of the literature in terms of dosimetry

Tibor Major^{1,2} · Georgina Fröhlich^{1,3} · Péter Ágoston^{1,2} · Csaba Polgár^{1,2} · Zoltán Takácsi-Nagy^{1,2}

The superiority of IRT is explained by its unparalleled dose distribution:

- low integral dose
- sharp dose gradient
- maximum OAR sparing
- high doses to tumor







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Review Article

Ann Transl Med 2017;5(10):207

External beam techniques to boost cervical cancer when brachytherapy is not an option-theories and applications

Omar Mahmoud^{1,2}, Sarah Kilic², Atif J. Khan^{1,2}, Sushil Beriwal³, William Small Jr⁴

The **applicator** inserted in the target volume eliminates the requirement of additional margins to account for set up error and/or to adapt to changes in bladder/rectal filling

The continuous non-systemic cervical motion can be as large as 18 mm



Mean interfractional cervical motion:

- 2.3-16 mm in the anterioreposterior
- 2.7-8 mm in the superior-inferior
- 0.3-10 mm in the lateral directions

Jadon. A systematic review of organ motion and image-guided strategies in external beam radiotherapy for cervical cancer. Clin Oncol 2014











Radioterapia di precisione per un'oncologia innovativa e sostenibile

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Omar Mahmoud^{1,2}, Sarah Kilic², Atif J. Khan^{1,2}, Sushil Beriwal³, William Small Jr⁴

Study	NGyn (cervical)	MFU (month)	Boost technique	WPI dose/dose per Fx	Boost dose/dose per Fx	Median OTT (days)	Tumor BED ₁₀₈	NT (rectal/bladder) $\text{BED}_{3\varepsilon}$	LC(%)*	> G2 Tax (%)*
Kagei <i>et al.</i> [2003] (65)	25 [25]	139	Proton	50.4/1.8	36/2.5-4	63	110	166	75	4
Park et al. [2004] (66)	10 [10]	18	3DCRT	50/2	30/5	NR	105	NR	60	0
Chan et al. [2006] (49)	12 [8]	23	3DCRT	45-50/1.8-2	25.2/1.8-2	63.5	85-90	NR	83	17
Matsuura et al. [2007] (67)	7 [7]	17	3DCRT	45/1.8	20-24/1.2-1.6®	42	80	NR	86	0
Barraciough et al. [2008](18)	44 [38]	27	3DCRT	40-45/2-2.5	15-25/1.8-2.5	54	66-87	91–128	79	2
Mazzola et al. [2016] (68)**	30 [30]	30	IMRT	54/1.8	66/2.2	NR	80.5	114	80	NR
Haas et al. [2012] (69)	6 [6]	14	SBRT (CK)	50.4-^61.2/1.8	19.5/6.5-20/4	NR	78-85	109/110°	100	0
Marnitz et al. [2013] (16)	11 [11]	6	SBRT(CK)	50.4/1.8	30/6	50	108	103/137	100	0
Kubicek et al. [2013] (70)	11 [4]	4	SBRT (CK)	45/1.8	25/5	NR	77	110	75	25
Hsieh et al. [2013] (71)	9 [9]	36	SBRT (HT)	50-50.4/2-1.8	16-27/2-4.5	79	91.2	197/189 ^e	78	0
Mantz [2016] (72)**	42 [30]	62	SBRT (NR)	45/1.8	40/8	NR	125	245	78.6	0

Limited number of studies evaluated high-tech EBRT as IRT alternative

- retrospective
- small population size
- various follow up time
- heterogeneous in dose
- heterogeneous in fractionation
- heterogeneous in technique









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SIB-RT vs SBRT



If IRT is deemed inadequate before starting CT-RT, **IMRT with SIB** should be the suggested technique to deliver the total dose in a shorter duration

Conversely, **SBRT** should be the preferred route in cases when IRT is deemed not applicable towards the end of the conventionally fractionated CT-RT regimen











Radioterapia di precisione per un'oncologia innovativa e sostenibile

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Omar Mahmoud^{1,2}, Sarah Kilic², Atif J. Khan^{1,2}, Sushil Beriwal³, William Small Jr⁴

The IMRT-SIB model may be preferred in the presence of **hypoxia** (hypoxic cells within cervical tumors 20–60%)



Adaptive replanning strategy to accentuate the precision by allowing modifications of the target volume due to bladder/rectal infill and/or any anticipated tumor shrinkage









IMRT with SIB





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Review Article

Ann Transl Med 2017;5(10):207

External beam techniques to boost cervical cancer when brachytherapy is not an option-theories and applications

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SBRT

SBRT is capable of **emulating HDR-IRT dose distribution** (high inhomogeneous dose to the tumor & OAR sparing)

The aim of **hypofractionation** is to target rapid cervical cancer cell repopulation through **avoiding overall treatment time** prolongation







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frontiers in ONCOLOGY

ORIGINAL RESEARCH ARTICLE published: 21 March 2012 doi: 10.3389/fonc.2012.00025

CyberKnife boost for patients with cervical cancer unable to undergo brachytherapy

Jonathan Andrew Haas^{1*}, Matthew R. Witten², Owen Clancey², Karen Episcopia², Diane Accordino¹ and Eva Chalas³

- 6 pts
- IMRT (pelvis) 45 Gy •
- IMRT (uterus) 50.4-61.2 Gy •
- SBRT-CK (cervix) 19.5-20 Gy in 3-5 fr ۲
- Fiducials (cervix and fornices)

CK

no G3-4



USA 2012











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Marnitz et al. Radiation Oncology 2013, 8:109 http://www.ro-journal.com/content/8/1/109



SHORT REPORT

Open Access

Brachytherapy-emulating robotic radiosurgery in patients with cervical carcinoma

Simone Marnitz^{1*}, Christhardt Köhler², Volker Budach¹, Oliver Neumann¹, Anne Kluge¹, Waldemar Wlodarczyk¹, Ulrich Jahn¹, Bernhard Gebauer³ and Markus Kufeld⁴





- 11 pts
- 3D-CRT 50.4 Gy
- SBRT-CK (cervix) 30 Gy in 5 fr
- Fiducials

- \Box
- LC @6 months 100%

CK

• no G3-4









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Germany 2013



Open Access

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Lee et al. Radiat Oncol (2021) 16:148 https://doi.org/10.1186/s13014-021-01877-4

Radiation Oncology

RESEARCH

Stereotactic ablative body radiotherapy boost for cervical cancer when brachytherapy boost is not feasible

Tae Hoon Lee¹, Changhoon Song², In Ah Kim², Jae-Sung Kim², Yong Beom Kim³, Kidong Kim³, Jae Hong No³, Dong Hoon Suh³, Jin-Beom Chung² and Keun-Yong Eom^{2*}



- 25 pts
- 3D-CRT/IMRT 44-50.4 Gy in 25-28 fr
- SBRT (VMAT) 20-33 Gy in 4-6 fr

VMAT

• median EQD2 75,5 Gy (69.3-92.2 Gy)



- LC @5yy 80.9%
- OS @5yy 69.4%







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Korea 2021



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Korea 2020

J Gynecol Oncol. 2020 Jul;31(4):e42



Comparing efficacy of high-dose rate brachytherapy versus helical tomotherapy in the treatment of cervical cancer

Seongmin Kim ^(C),¹² Sanghoon Lee ^(C),² Jin Hwa Hong ^(C),² Young Je Park ^(C),³ Jae Yun Song ^(C),² Jae Kwan Lee ^(C),² Nak Woo Lee ^(C),²





matched population 70 IRT pts vs 35 HT pts

- 3D-CRT 45-54 Gy
- SBRT (HT) 30 Gy in 10 fr
- HDR IRT 24-30 Gy in 6 fr





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- PFS @5-yy

- OS @5-yy

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IRT 72.6%

HT 72.5%

IRT 78%

HT 76.5%





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Tumor Boost Using External Beam Radiation in Cervical Cancer Patients Unable to Receive Intracavitary Brachytherapy Outcome From a Multicenter Retrospective Study (Korean Radiation Oncology Group 1419)

Haeyoung Kim, MD,* Young Seok Kim, MD,† Ji Hyeon Joo, MD,† Keun-Yong Eom, MD,‡ Won Park, MD,§ Jin Hee Kim, MD,// Jong Hoon Lee, MD,¶ Yeon Sil Kim, MD,# Seok Ho Lee, MD,** Kijung Ahn, MD,†† Yong Bae Kim, MD,‡‡ Me-Yeon Lee, MD,§§ and Sei Kyung Chang, MD////

(Int J Gynecol Cancer 2018;28: 371-378)

- 75 pts (multicentric)
- 3D-CRT box (pelvis) 40-54 Gy
- 3D-CRT / IMRT 9 35 Gy
- median EQD2 70 Gy (49.6-80.7 Gy)



Korea 2018



- G3-4 12%
- LC @5-yy 70%
- DFS @5-yy 54.7%
 - OS @5-yy 75%

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Clinical Investigation

Int J Radiation Oncol Biol Phys, Vol. 106, No. 3, pp. 464-471, 2020

A Phase II Trial of Stereotactic Ablative Radiation Therapy as a Boost for Locally **Advanced Cervical Cancer**

Kevin Albuquerque, MD,*^{,†} Vasu Tumati, MD,* Jayanthi Lea, MD,^{†,‡} Chul Ahn, PhD,[§] Debra Richardson, MD,^{†,‡} David Miller, MD,^{†,‡} and Robert Timmerman, MD*/

- phase II trial
- 15/21 pts: closed for toxicity
- IMRT 45 Gy
- SBRT 28 Gy in 4 fr (fiducials) •





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<u>G5 3 pts</u>

- LC @2yy 70.1%
- PFS @2yy 46.7%
- OS @2yy 53.3%







Local Control

12 15

Months

18

21 24

9

100

75

50

25

0

3

USA 2020

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	Gynecologic Oncology 152 (2019) 540-547	
	Contents lists available at ScienceDirect	STNECOLOGIC
\$~52 E	Gynecologic Oncology	CNCCLOST
ELSEVIER	journal homepage: www.elsevier.com/locate/ygyno	() <u> </u>
Brachytherapy: cervical cancer	A critical component of primary radiation therapy for	Check for spelates
From the Society	of Gynecologic Oncology (SGO) and the American Bra	chytherapy
Society (ABS)		

Christine H. Holschneider ^{a,*}, Daniel G. Petereit ^b, Christina Chu ^c, I-Chow Hsu ^d, Yevgeniya J. loffe ^e, Ann H. Klopp ^f, Bhavana Pothuri ^g, Lee-may Chen ^h, Catheryn Yashar ⁱ

The declining utilization of IRT is coupled with increased mortality risk





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USA 2021

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•

•

37 pts

Japanese Journal of

Japanese Journal of Clinical Oncology, 2019, 49(3) 270-275 doi: 10.1093/jico/hvv187 Advance Access Publication Date: 20 December 2018 Original Article

Original Article

Clinical outcomes following conventional external beam radiotherapy boost in Japanese patients with cervical cancer who are ineligible for intracavitary brachytherapy

Kei Ito*, Takuya Shimizuguchi, and Katsuyuki Karasawa



Japan 2019

PFS @2-yy 29% OS @ 2-yy 43%

3D-CRT pelvis + 3D-CRT boost

Total dose 56 - 70 Gy



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Intensity modulated radiation therapy boost in locally-advanced cervical cancer in the absence of brachytherapy

Int J Gynecol Cancer 2020;30:607-612.

Roberta Lazzari,¹ Giulia Riva,² Matteo Augugliaro,¹ Andrea Vavassori,¹ Samantha Dicuonzo,¹ Federica Cattani,³ Stefania Comi,³ Nicoletta Colombo,⁴ Barbara Alicja Jereczek-Fossa^{1,5}



Milano 2020

- 25 pts
- 3D-CRT / IMRT (pelvis) 45 50.4 Gy
- SBRT (cervix) 25 Gy in 5 fr

- No G3-4
- LC @2-yy 78%
- PFS @2-yy 55%
- OS @2-yy 67%





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Radioterapia di precisione per un'oncologia innovativa e sostenibile

CANCER DIAGNOSIS & PROGNOSIS

1: 53-60 (2021)

doi: 10.21873/cdp.10008

Stereotactic Body Radiation Therapy Boost in Patients With Cervical Cancer Ineligible for Brachytherapy

GIUSEPPE FACONDO*, GIANLUCA VULLO*, VITALIANA DE SANCTIS, MAURIZIO VALERIANI, ANNA MARIA ASCOLESE, MARIA MASSARO, DIMITRI ANZELLINI and MATTIA FALCHETTO OSTI

- 9 pts
- IMRT (pelvis) 50.4 + SIB (cervix +/- N) 61.6 Gy
- SBRT (cervix) 15-25 Gy in 3-5 fr
- median EQD2 80.8-92.4 Gy

- 1 pt local recurrence
- 2 pts PD
 - OS @2-yy 70%

















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Salvage treatment or reirradiation





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Contents lists available at ScienceDirect Taiwanese Journal of Obstetrics & Gynecology

Taiwanese Journal of Obstetrics & Gynecology 60 (2021) 111-118

journal homepage: www.tjog-online.com

Original Article

Stereotactic body radiotherapy for pelvic boost in gynecological cancer patients with local recurrence or unsuitable for intracavitary brachytherapy

Hsin-Yi Cheng ^a, Ji-An Liang ^{a, b}, Yao-Ching Hung ^{b, d}, Lian-Shung Yeh ^d, Wei-Chun Chang ^{b, d}, Wu-Chou Lin ^{b, d, e}, Shang-Wen Chen ^{a, b, c, *}

- 11 pts cervix/uterus
- 3D-CRT 45-65 Gy
- SBRT 25 Gy in 5 fr



Taiwan 2021



• G3-4 2 pts



- 14 **recurrent** cancer (5 reirradiation)
- 3D-CRT 50-65 Gy
 - SBRT 10-30 Gy in 2-6 fr



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49.1% rec

OS @1yy 80.8% def

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Radioterapia di precisione per un'oncologia innovativa e sostenibile

Radiation Oncology (2022) 17:8 https://doi.org/10.1186/s13014-022-01981-2 RESEARCH Open Access MR-guided SBRT boost for patients with locally advanced or recurrent gynecological cancers ineligible for brachytherapy: feasibility and early clinical experience

Indrawati Hadi¹, Chukwuka Eze¹¹¹, Stephan Schönecker¹, Rieke von Bestenbostel¹, Paul Rogowski¹, Lukas Nierer¹, Raphael Bodensohn¹, Michael Reiner¹, Guillaume Landry¹, Claus Belka^{1,2}, Maximilian Niyazi^{1,2} and Stefanie Corradini¹

Germany 2022



- 10 pts (8 recurrent cervical / vaginal cancer)
- VMAT 45-55 Gy in 25 fr
- MRI-SBRT median 21 Gy in 4 fr
- median EQD2 73.6 Gy (69.3-83.9 Gy)

- no G3-4
- LC @5yy 80.9%
- OS @5yy 69.4%













Radioterapia di precisione per un'oncologia innovativa e sostenibile

A new possibility: PROTON & CARBON ION











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Radioterapia di precisione per un'oncologia innovativa e sostenibile

Int J Radiation Oncol Biol Phys, Vol. 87, No. 5, pp. 897-903, 2013

Intensity Modulated Proton Beam Radiation for Brachytherapy in Patients With Cervical Carcinoma

Alessandro Clivio, MSc,* Anne Kluge, MSc,[†] Luca Cozzi, PhD,* Christhardt Köhler, MD,[‡] Oliver Neumann, MD,[†] Eugenio Vanetti, MSc,* Waldemar Wlodarczyk, MD,[†] and Simone Marnitz, MD[†]

- 11 pts (cervical cancer)
- IMRT (VMAT or Helical) 50.4 Gy
- SBRT (CK) 30 Gy in 5 fr
- median EQD2 89.6 Gy

As an alternative

- IMPT 30 Gy in 5 fr
- Reference comparison plans with VMAT





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BOLOGNA, 25-27 NOVEMBRE

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Radioterapia di precisione per un'oncologia innovativa e sostenibile



Personalized treatment adaptation for improved treatment efficacy









Società Italiana di Radiobiologia





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CONCLUSIONS

Italy 2021



High-tech EBRT may be suitable only for carefully selected patients

Image guided IRT still remains the clear standard of care and efforts should be made to maintain expertise and skills







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TAKE-HOME MESSAGE

Instead of comparing them, future studies should focus on **combining advanced EBT and advanced IRT** by using the inherent advantages of both options, to fully exploit the potential of advanced RT







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