Interventional radiotherapy in the adaptive management: Head and Neck Cancer

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Gemelli ART (Advanced Radiation Therapy) - Interventional Oncology Center (IOC)

10th October 2023

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Fondazione Policlinico Universitario Agostino Gemelli IRCCS
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Interventional and External beam
INTERACTS
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Adaptive Interventional Radiotherapy (Brachytherapy): What?

Phys. Med. Biol. **42** (1997) 123–132. Printed in the UK PII: S0031-9155(97)67292-9

Adaptive radiation therapy

Di Yan†, Frank Vicini, John Wong and Alvaro Martinez
Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI 48073, USA

Received 11 August 1995, in final form 29 August 1996

Abstract. Adaptive radiation therapy is a closed-loop radiation treatment process where the treatment plan can be modified using a systematic feedback of measurements. Adaptive radiation therapy intends to improve radiation treatment by systematically monitoring treatment variations and incorporating them to re-optimize the treatment plan early on during the course of treatment. In this process, field margin and treatment dose can be routinely customized to each individual patient to achieve a safe dose escalation.

Monitoring treatment variations

- Patient set-up
- Anatomical changes
- Tumor shrinkage

Safe dose escalation

Adaptive Interventional Radiotherapy (Brachytherapy): Why?

Educational Activity

Review paper

Modern head and neck brachytherapy: from radium towards intensity modulated interventional brachytherapy

György Kovács, MD, PhD

Interdisciplinary Brachytherapy Unit, University of Lübeck/University Hospital Schleswig-Holstein Campus Lübeck, Germany

Table 2. Representative brachytherapy results in oral cavity cancer (LDR/HDR/PDR)

Author	*n*	Anatomic site	Dose (Gy)	LDR	HDR	PDR	5 years local control (%)	5 years OS (%)	Toxicity
Pernot *et al.* [35]	552	Mobile tongue	70-75	^{192}Ir, wire	–	–	St. I: 95 St. II: 65 St. III: 54 St. IV: 36	St. I: 71 St. II: 43 St. III: 33 St. IV: 23	Grade I: 20% Grade II: 9% Grade III: 4% Grade IV: 0.2%
Pernot *et al.* [35]	207	Floor of mouth	70-75	^{192}Ir, wire	–	–	St. I: 97 St. II: 73 St. III: 64 St. IV: 0	St. I: 74 St. II: 46 St. III: 39 St. IV: 0	Grade I: 20% Grade II: 9% Grade III: 4% Grade IV: 0.2%
Yoshida *et al.* [46]	70	Mobile tongue	70	^{192}Ir ^{226}Ra ^{60}Co	–	–	78 71 (10 yrs)	80 CSS 72 (10 yrs) CSS	n.d.
Inoue *et al.* [39]	58	Mobile tongue	6 × 10	–	HDR	–	T1/T2 = 82/79	T1/T2 = 83/82, CSS	10%
Inoue *et al.* [39]	341	Mobile tongue	70	^{192}Ir ^{226}Ra	–	–	T1/T2 = 85/80	T1/T2 = 85/79, CSS	6%
Marsiglia *et al.* [49]	160	Floor of mouth	60-70	^{192}Ir, wire	–	–	T1/T2 = 93/88	76	18% bone necrosis 10% soft tissue necrosis
Strnad *et al.* [62]	67	Floor of mouth	50-64	–	–	PDR 24 hours	Approx. 87	Approx. 77	9.7% soft tissue necrosis 7.2% bone necrosis
Strnad *et al.* [62]	103	Mobile tongue	50-64	–	–	PDR 24 hours	Approx. 78	Approx. 67	9.7% soft tissue necrosis 7.2% bone necrosis
Guinot *et al.* [43]	50	Mobile tongue	11 × 4	–	HDR IMBT bid	–	79	70	4% bone necrosis 16% soft tissue necrosis
Yamazaki *et al.* [45]	80	Mobile tongue	6 × 10	–	HDR bid	–	T1/T2/T3 82/79/89	T1/T2/T3, CSS 86/781/89	T1/T2/T3 17%/20%/0%

LDR – low-dose-rate, HDR – high-dose-rate, PDR – pulsed-dose-rate, OS – overall survival, CSS – cause specific survival, bid – twice a day fractions (min. 6 hours interval), IMBT – intensity modulated brachytherapy

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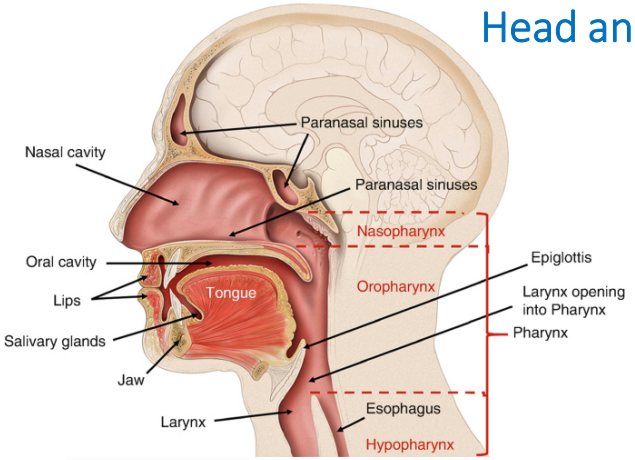
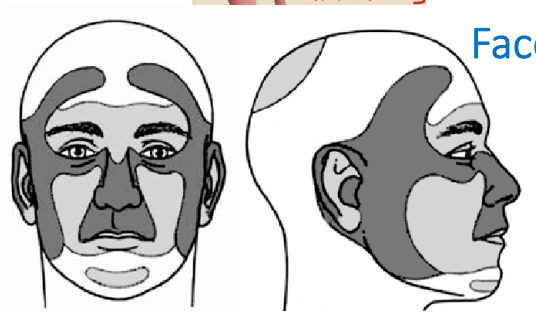
ART Advanced Radiation Therapy

Adaptive Interventional Radiotherapy (Brachytherapy): Where?

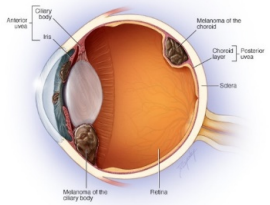
Head and Neck

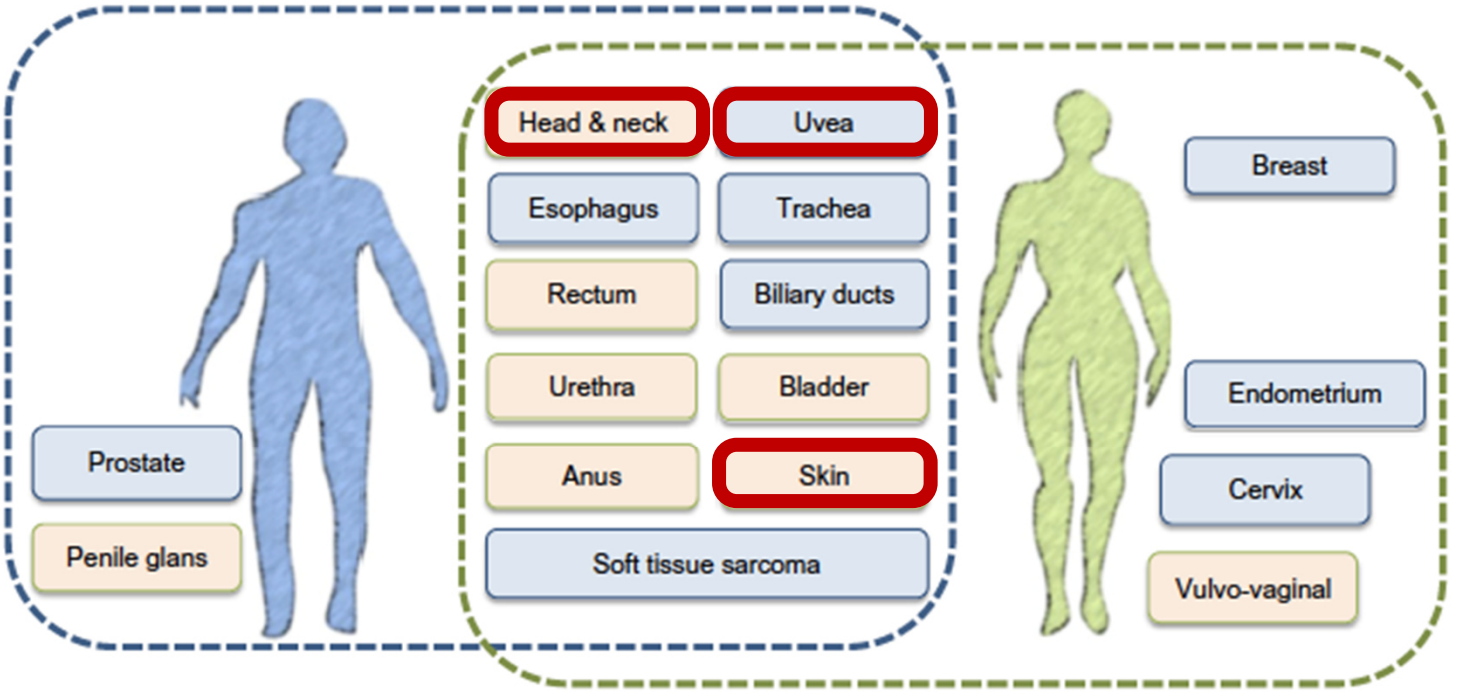


Face Skin



Eye





Indications based on randomized control rials

Indications based on retrospective cohort studies

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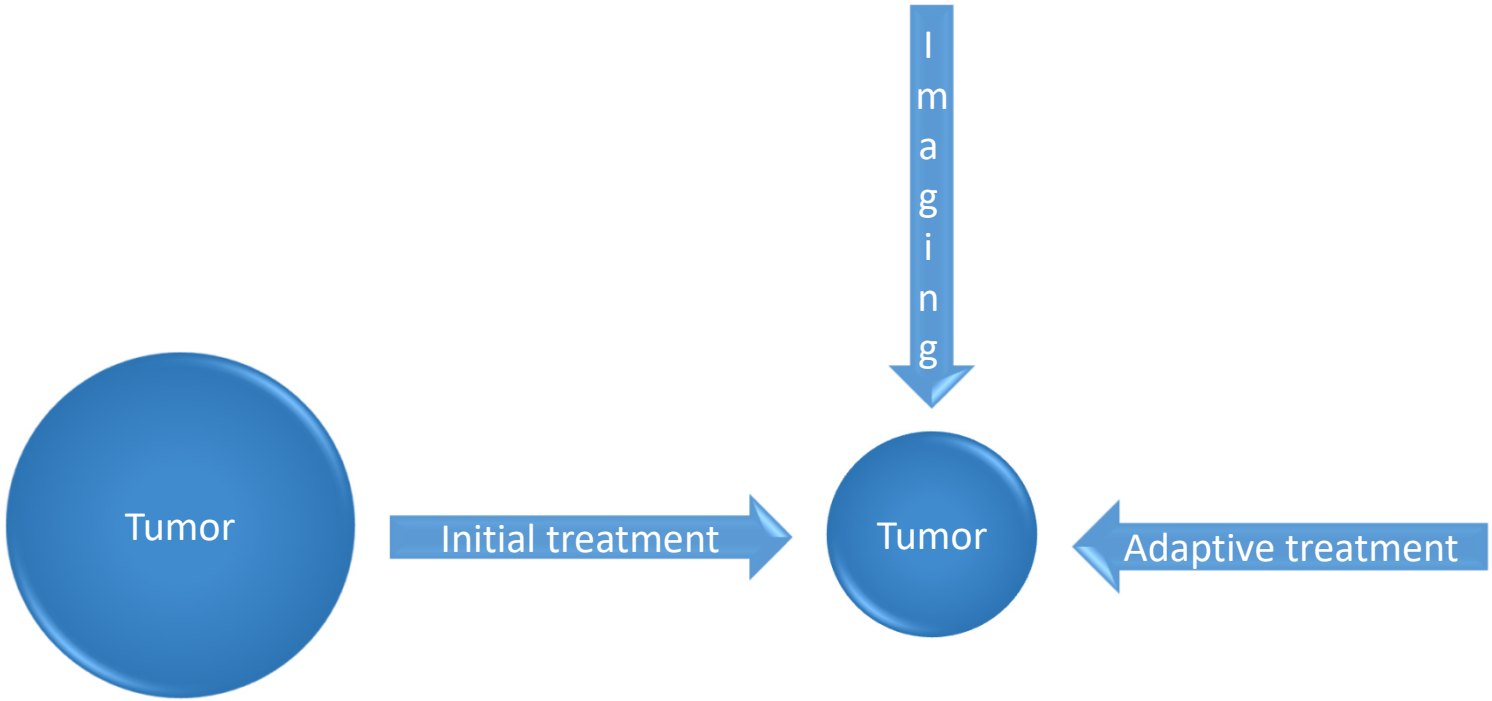
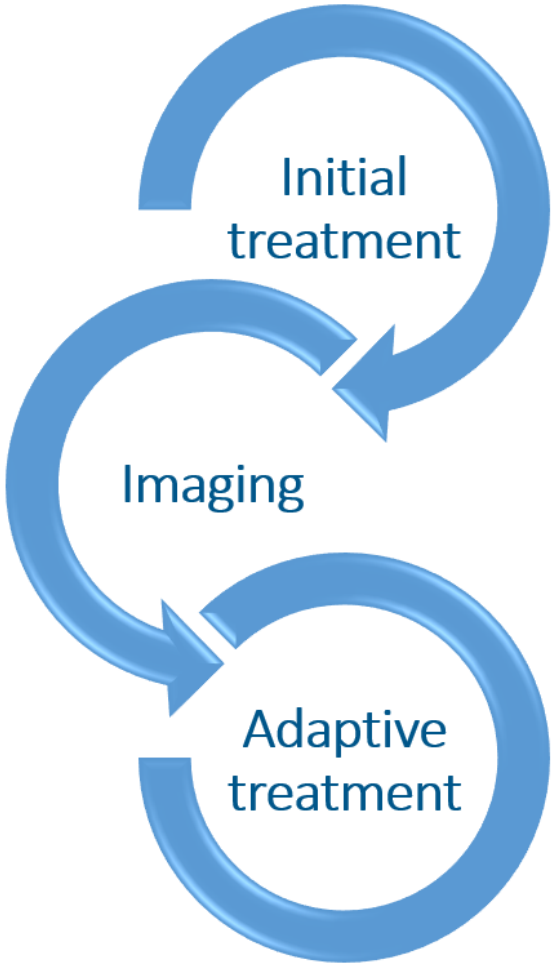
ART Advanced Radiation Therapy

Cyrus Chargari, Eric Deutsch, Pierre Blanchard, Sebastien Gouy, Hélène Martelli, Florent Guérin, Isabelle Dumas, Alberto Bossi, Philippe Morice, Akila N. Viswanathan, Christine Haie-Meder, Brachytherapy: An Overview for Clinicians CA CANCER J CLIN 2019

Adaptive Interventional Radiotherapy (Brachytherapy): When?



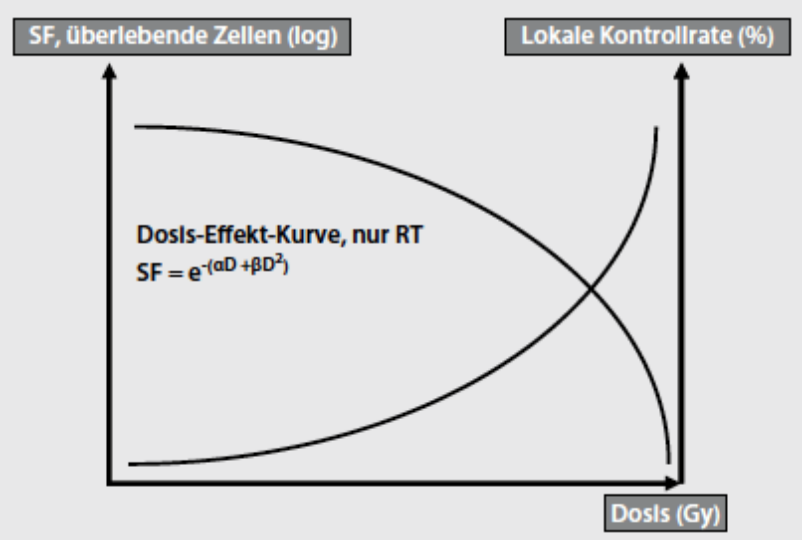
Adaptive Interventional Radiotherapy (Brachytherapy): How?



- Radiotherapy +/- chemotherapy
  - Biological therapy
  - Immunotherapy
  - Other therapies
- MRI, CT, CT-PET, US
- Intensity modulation (Contact/Interstitial)

Local control

RT DOSE → LOCAL CONTROL → ORGAN PRESERVATION



Gerbaulet A, Pötter R, Mazeron JJ, et al. The GEC ESTRO handbook of brachytherapy. Brussels**: ESTRO publisher; 2002**
Meyer JE, Brocks C, Maune S, Strnad V, Werner JA, Wollenberg B, Kovács G. Brachytherapy for the treatment of head and neck cancer - **HNO. 2010**

Contents lists available at ScienceDirect

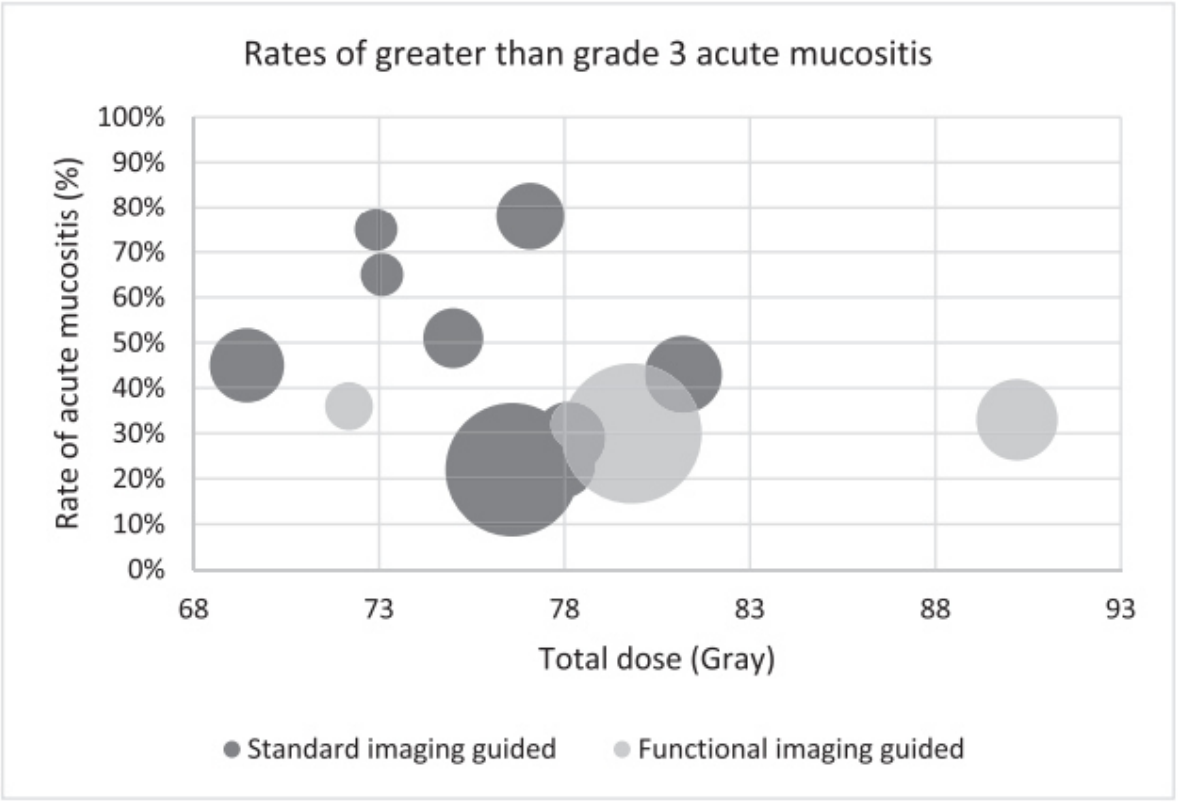
Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Overview

A Review of Modern Radiation Therapy Dose Escalation in Locally Advanced Head and Neck Cancer

D. Atwell *†‡, J. Elks ‡, K. Cahill *‡, N. Hearn *†‡, D. Vignarajah *†, J. Lagopoulos ‡, M. Min *†‡



(A)

Clinical Oncology
Volume 35, Issue 8, August 2023, Pages 497-506

Function Preservation in Head and Neck Cancers

A. Budrukkar *, J.L. Guinot †, L. Tagliaferri ‡, F. Bussu §¶, A. García-Consuegra ||, G. Kovacs **

- ✓ Due to the rapid fall-off of the dose of interventional radiotherapy (brachytherapy) there is better organ at risk sparing as compared with that of external beam radiotherapy
- ✓ Interventional radiotherapy (brachytherapy) in oropharyngeal cancers has been shown to reduce xerostomia and also reduce dysphagia and aspiration post-radiation therapy
- ✓ For the nasopharynx and nose vestibule interventional radiotherapy (brachytherapy) preserves the respiratory function of the mucosa

Journal of *Personalized Medicine*

MDPI

Article

ORIFICE (Interventional Radiotherapy for Face Aesthetic Preservation) Study: Results of Interdisciplinary Assessment of Interstitial Interventional Radiotherapy (Brachytherapy) for Periorificial Face Cancer

Luca Tagliaferri [1], Ilaria Giarrizzo [2], Bruno Fionda [1,*], Mario Rigante [3], Monica Maria Pagliara [4], Calogero Casà [1], Claudio Parrilla [3], Valentina Lancellotta [1], Elisa Placidi [1], Alessandra Salvati [2], Gabriella Macchia [5], Stefano Gentileschi [6,7], Maria Antonietta Blasi [4,8], Alessio Giuseppe Morganti [9,10], Francesco Bussu [11,12], Ketty Peris [13,14], Gaetano Paludetti [3,15] and Vincenzo Valentini [1,2]

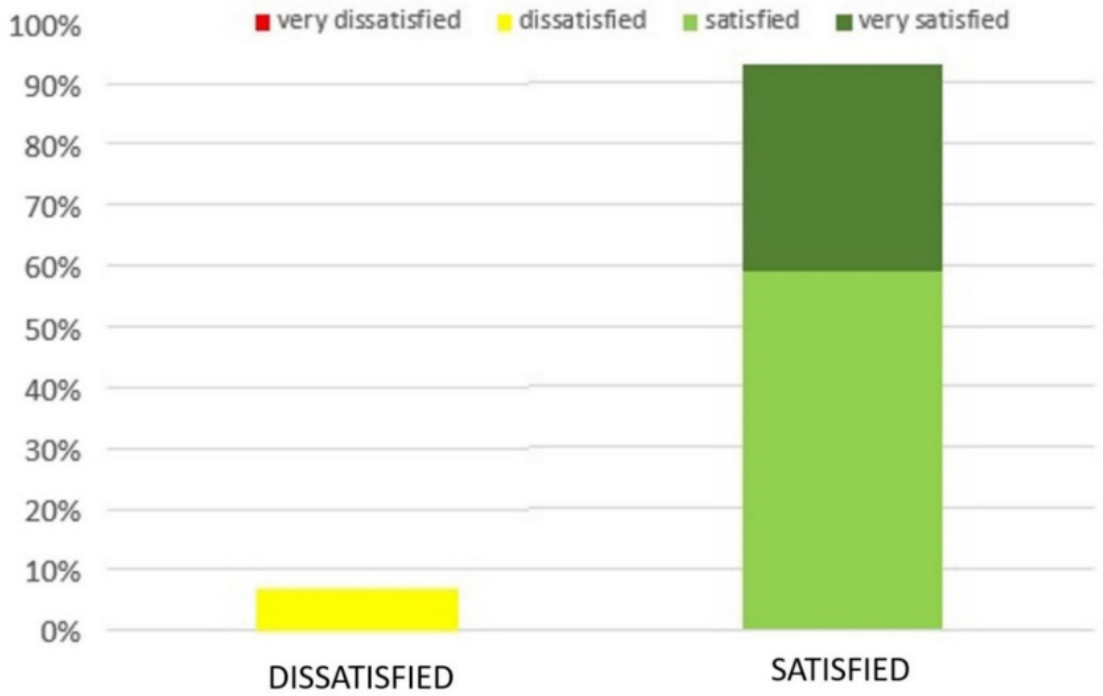
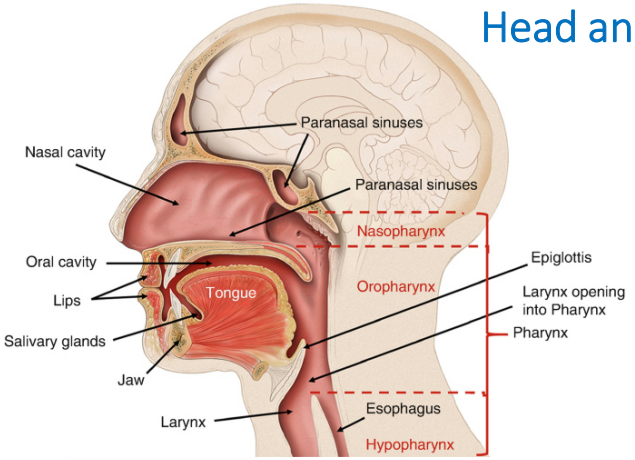
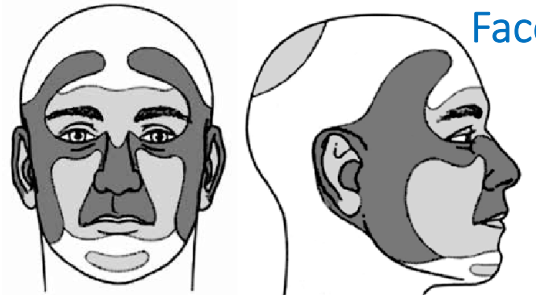


Figure 2. Patients' satisfaction after treatment with IRT.

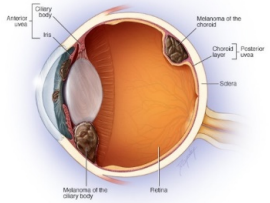
Head and Neck



Face Skin



Eye



Organ sparing

Function sparing

Cosmesis Sparing

Initial Treatment

Radiotherapy and Oncology 122 (2017) 248–254

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

GEC-ESTRO/ACROP recommendations

GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: 1st update – Improvement by cross sectional imaging based treatment planning and stepping source technology

György Kovács [a,*,1], Rafael Martinez-Monge [b,1], Ashwini Budrukkar [c,1], Jose Luis Guinot [d,1], Bengt Johansson [e,1], Vratislav Strnad [f,1], Janusz Skowronek [g,h,1], Angeles Rovirosa [i,1], Frank-André Siebert [j,1], on behalf of the GEC-ESTRO Head & Neck Working Group

Combined ERT and IRT is an acceptable mode of treatment in

1) in T1-2 tumors in patients ineligible for surgery

2) In advanced T3-4 and tumors that would require surgical resections with functional or cosmetic impact (i.e. base of tongue)

3) In other locations eligible for primary radiotherapy in whom a IRT boost outweighs the discomfort of a surgical procedure (i.e. nasopharynx)

The Journal of Laryngology & Otology (2016), ***130*** (Suppl. S2), *S28–S31*.

doi:10.1017/S0022215116000396

GUIDELINE

Imaging

Imaging in head and neck cancer: United Kingdom National Multidisciplinary Guidelines

H LEWIS-JONES[1], S COLLEY[2], D GIBSON[3]

[1]Department of Radiology, University Hospital Aintree, Liverpool, [2]Department of Radiology, University Hospital Birmingham NHS Trust, Birmingham, UK, and [3]Fiona Stanley Hospital, Murdoch, Perth, WA, Australia

Abstract

This guideline is endorsed by the specialty associations involved in the care of head and neck cancer patients in the UK. This paper summarises the current imaging modalities in use for head and neck cancer evaluation. It highlights their role in the management with recommendations on modality choice for each cancer subsite.

Recommendations

- Offer appropriate radiological imaging, based on tumour extent, site and local expertise, to stage tumours and plan treatment for patients diagnosed with head and neck cancer. (G)
- Consider positron emission tomography combined with computed tomography (PET–CT) imaging if conventional cross-sectional imaging identifies no primary site. (R)
- Offer PET–CT imaging 12 weeks after non-surgical treatment to detect residual disease. (R)

Interstitial IRT

Embring *et al. Radiation Oncology* (2023) 18:65
https://doi.org/10.1186/s13014-023-02256-x

Radiation Oncology

RESEARCH Open Access

Dose escalation in oropharyngeal cancer: a comparison of simultaneous integrated boost and brachytherapy boost

Anna Embring[1,2*], Eva Onjukka[1,3], Claes Mercke[1,2], Ingmar Lax[1,3], Anders Berglund[4] and Signe Friesland[1,2]

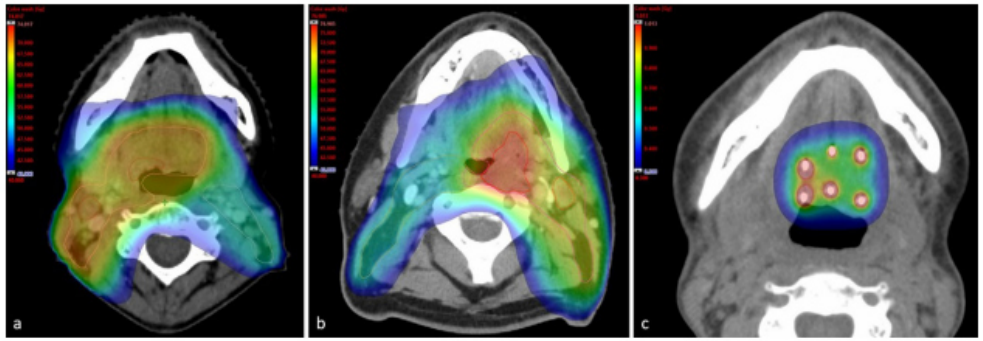


Fig. 1 Pictures of dose distribution in colour wash. **a** Picture with an example of external beam radiotherapy with standard dose to high-risk volumes and contralateral elective lymph node irradiation. **b** Picture with an example of a simultaneous integrated boost with dose escalation to the primary tumour, standard dose to high-risk volumes and contralateral elective lymph node irradiation. **c** Picture with an example of a brachytherapy boost

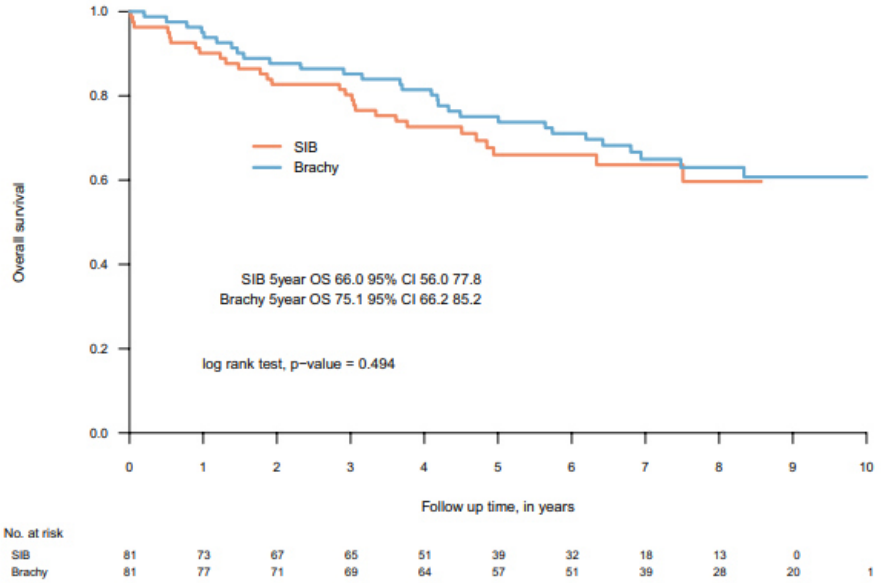


Fig. 3 Propensity score matched overall survival by boost modality. SIB—simultaneous integrated boost, Brachy—brachytherapy boost in combination with external beam radiotherapy

Interstitial IRT

International Journal of Radiation Oncology*Biology*Physics
Available online 2 September 2023
In Press, Journal Pre-proof What's this?

Clinical Investigation

Intensity Modulated Radiation Therapy Alone Vs Intensity Modulated Radiation Therapy and Brachytherapy for T1-T2N0M0 Oropharyngeal Cancers: Results from A Randomized Controlled Trial

Ashwini Budrukkar MD [1], Vedang Murthy MD [2], Sheetal Kashid MD [1], Monali Swain MD [1], Venkatesh Rangarajan MD [3], Sarbani Ghosh Laskar MD [1], Sadhana Kannan MSc [4], Shrikant Kale MSc [5], Rituraj Upreti PhD [5], Prathamesh Pai MS [6], Gouri Pantvaidya MS [6], Tejpal Gupta MD [2], Jai Prakash Agarwal MD [1]

- ✓ Patients with stage I and II OPSCC were considered for IMRT to a dose of 50Gy/25#/5 weeks in phase I followed by randomization (1:1) to further treatment with IMRT (20Gy/10#/2 weeks) or BT (192Ir high dose rate - 21Gy/7fractions/2 fractions per day)
- ✓ Severe salivary toxicity (xerostomia) was defined as post-treatment salivary excretion fraction ratio <45%
- ✓ Between November 2010 to February 2020, 90 patients were randomized to IMRT(N=46) alone or IMRT+BT(N=44)
- ✓ At 6 months, xerostomia rates using salivary scintigraphy were 14% (5/35: 95% CI 5%-30%) in the BT arm while it was seen in 44% (14/32: 95%CI 26%-62%) in the IMRT arm (p=0.008)
- ✓ At a median follow-up of 42.5 months, the 3-year LC in the IMRT arm was 56.4% (95% CI-43%-73%) while it was 66.2% (95% CI: 53%-82%) in the BT arm (P=0.24)

Contact IRT

Reports of Practical Oncology and Radiotherapy 25 (2020) 479–483

Available online at www.sciencedirect.com

Reports of Practical Oncology and Radiotherapy

journal homepage: http://www.elsevier.com/locate/rpor

Should high-dose-rate brachytherapy boost be used in early nasopharyngeal carcinomas?

Jose Luis Guinot[a,⁎], Andrea Moya[a], Miguel Angel Santos[a], Marina Peña[a], Beatriz Quiles[a], Juan Carlos Sanchez-Relucio[b], Alonso La Rosa[a], Maria Isabel Tortajada[a], Leoncio Arribas[a]

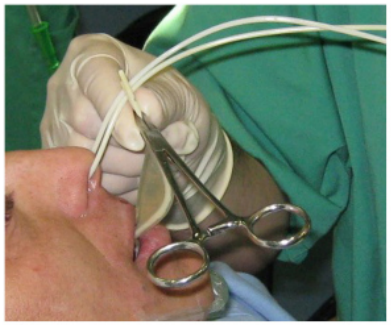


Fig. 1. Placement of Rotterdam applicator.

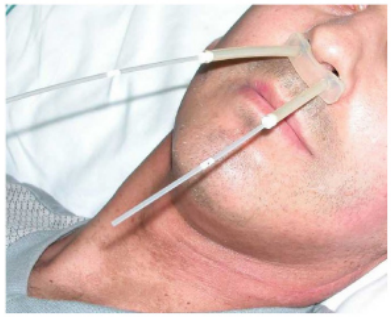


Fig. 2. Rotterdam applicator in site.

Fig. 3. Lateral view with dummy sources.

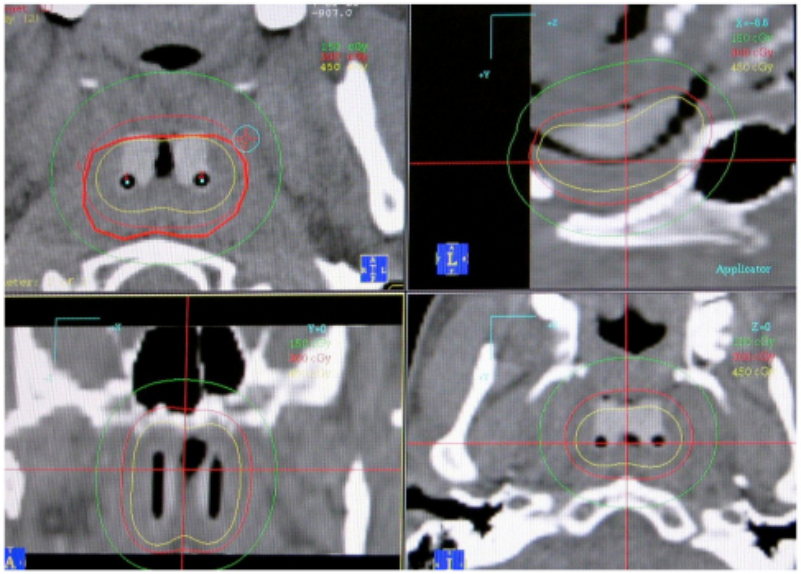
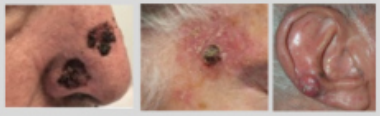


Fig. 4. CTV and isodose curves.

Initial Treatment

Table 1 EADO staging system for BCC

Risk	Stage		Characteristics		Illustrative pictures	DTT-BCC Group (part 1)
Easy To Treat and low risk of recurrence	Common BCC	I	Low-risk common BCC	**None of the other stages characteristics.** *Recurrences only come from blind treatments, or insufficient surgical margins.*		*Not included*
Increasingly Difficult To Treat and increasing risk of recurrence	Common BCC	IIA	Common BCC but somewhat DTT	Common BCC but management is more complex than usual for any reason linked to the tumor (location requiring technical skill, poorly defined tumor borders, prior recurrence) and/or to the patient (poor general status, comorbidities, or unwillingness to cooperate ...). *Good results and low rate of recurrence expected with surgery even if technically complicate, when the patient cooperates.*		*1*
	Common BCC	IIB	DTT-BCC mainly due to multiplicity of common BCC	Very high number of common BCC (>10) or multiple complex BCC (> 5) in the setting of apparently sporadic cases or in Gorlin syndrome*. *When at least 1 of the multiple BCC can be classified III or IV, the patient will be classified accordingly, and not IIB		*2*
	Advanced BCC	IIIA	Locally advanced DTT-BCC out of critical areas	Large and/or destructive tumors in non-critical or functionally significant areas. *Deemed curable without expected functional mutilations.*		*3*
	Advanced BCC	IIIB	Locally advanced DTT-BCC in critical areas	Large and/or or destructive tumors in critical or functionally important areas (periorificial, nose, ...). *Deemed curable by surgery, but functional impairment and/or mutilation are inevitable.*		*4*
	Advanced BCC	IIIC	Extremely advanced DTT- BCC	Giant and/or deeply invasive tumors involving extracutaneous tissue (bone, muscles, vital or sensorial structures) responsible for an extreme clinical situation. *Cure cannot be expected by surgery whatever its extent.*		*5*
	Metastatic BCC	IV		Distant metastases*. *Whatever the initial BCC staging, patient must be classified IV when metastatic.		*Not included*

The Oncologist®

Melanoma and Cutaneous Malignancies

Hedgehog Inhibitor Induction with Addition of Concurrent Superficial Radiotherapy in Patients with Locally Advanced Basal Cell Carcinoma: A Case Series

Joshua P. Weissman,[a,b] Wolfram Samlowski,[b,c,d] Raul Meoz[b,c,d]

[a]Feinberg School of Medicine, Northwestern University, Evanston, Illinois, USA; [b]Comprehensive Cancer Centers of Nevada, Las Vegas, Nevada, USA; [c]School of Medicine, University of Nevada, Las Vegas, Las Vegas, Nevada; [d]University of Nevada School of Medicine, Reno, Nevada, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Non-melanoma skin cancer • Keratinocyte carcinoma • Sonidegib • Vismodegib

Initial Treatment

Figure 1. A large locally advanced basal cell carcinoma of the left temple pretreatment (**A**). Radiation field and shielding after 2.5 months hedgehog inhibitor (HHI) therapy (**B**). Treatment response at 52 months after HHI and radiotherapy (**C**).

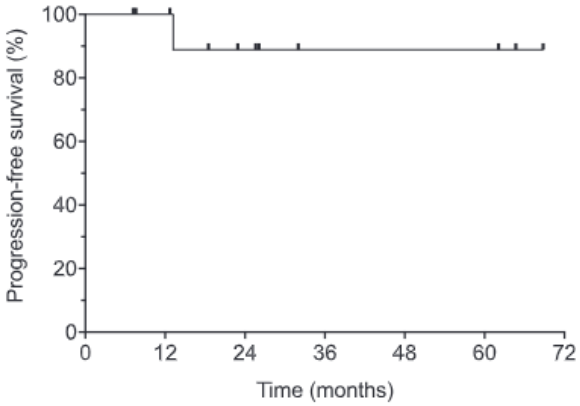


Figure 3. Progression-free survival of patients treated with induction hedgehog inhibitor therapy with subsequent addition of radiotherapy consolidation. Hash marks indicate censored patients.

Initial Treatment

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

First-In-Human Study of Cemiplimab Alone or In Combination with Radiotherapy and/or Low-dose Cyclophosphamide in Patients with Advanced Malignancies

Kyriakos P. Papadopoulos[1], Melissa L. Johnson[2], Albert C. Lockhart[3], Kathleen Moore[4], Gerald S. Falchook[5], Silvia C. Formenti[6], Aung Naing[7], Richard D. Carvajal[8], Lee S. Rosen[9], Glen J. Weiss[10], Rom S. Leidner[11], Jingjin Li[12], Anne Paccaly[13], Minjie Feng[12], Elizabeth Stankevich[12], Israel Lowy[13], Matthew G. Fury[13], and Marka R. Crittenden[14]

frontiers in Oncology

ORIGINAL RESEARCH
published: 08 November 2021
doi: 10.3389/fonc.2021.686308

Cemiplimab in an Elderly Frail Population of Patients With Locally Advanced or Metastatic Cutaneous Squamous Cell Carcinoma: A Single-Center Real-Life Experience From Italy

OPEN ACCESS

Edited by:
Wen-Qing Li,
Peking University Cancer

Sabino Strippoli[1], Annarita Fanizzi[2], Davide Quaresmini[1], Annalisa Nardone[3], Andrea Armenio[4], Francesco Figliuolo[4], Raffaele Filotico[5], Livia Fucci[6], Fabio Mele[6], Michele Traversa[7], Federica De Luca[7], Elisabetta Sara Montagna[8], Eustachio Ruggieri[9], Simona Ferraiuolo[10], Francesco Macina[11], Stefania Tommasi[12], Angela Monica Sciacovelli[1], Ivana De Risi[1], Anna Albano[1], Raffaella Massafra[2] and Michele Guida[1]*

cancers

MDPI

Article

Real-Life Study of the Benefit of Concomitant Radiotherapy with Cemiplimab in Advanced Cutaneous Squamous Cell Carcinoma (cSCC): A Retrospective Cohort Study

Barbara Bailly-Caillé [1,*], Diane Kottler [1], Rémy Morello [2], Marie Lecornu [3], William Kao [4], Emmanuel Meyer [5], Anne Dompmartin [1] and Jean-Matthieu L'Orphelin [1]

Oncol Ther (2021) 9:153–166
https://doi.org/10.1007/s40487-021-00138-4

ORIGINAL RESEARCH

The Treatment of Non-Melanoma Skin Cancer with Image-Guided Superficial Radiation Therapy: An Analysis of 2917 Invasive and In Situ Keratinocytic Carcinoma Lesions

Lio Yu · Chad Oh · Christopher R. Shea

Imaging

Key Summary Points

Image Guided Superficial Radiation Therapy (IGSRT) was safe and well tolerated in this study, involving 1632 patients with non-melanoma skin cancer (NMSC). Of 2917 NMSC lesions treated, local tumor control was achieved in 2897 lesions, representing a 99.3% rate of control.

IGSRT should be considered as a first-line option for treating stage 0–II NMSC lesions in suitable patients, especially those who are not candidates for surgery or who decline surgery.

NMSC is a highly prevalent condition, with an estimated annual incidence in the U.S. of 5.5 million tumors in 2012.

This study presents a retrospective evaluation of efficacy and safety of image-guided superficial radiotherapy, a nonsurgical treatment option, in 2917 NMSC lesions (1632 patients).

Treatment with IGSRT resulted in local tumor control in 2897 lesions, representing a 99.3% rate of control.

IGSRT was safe and well-tolerated in this study.

These results suggest IGSRT should be considered as a first-line option for treating NMSC in suitable patients.

Contact IRT

Technical Note

Original paper

Multilayer intensity modulated contact interventional radiotherapy (brachytherapy): Stretching the therapeutic window in skin cancer

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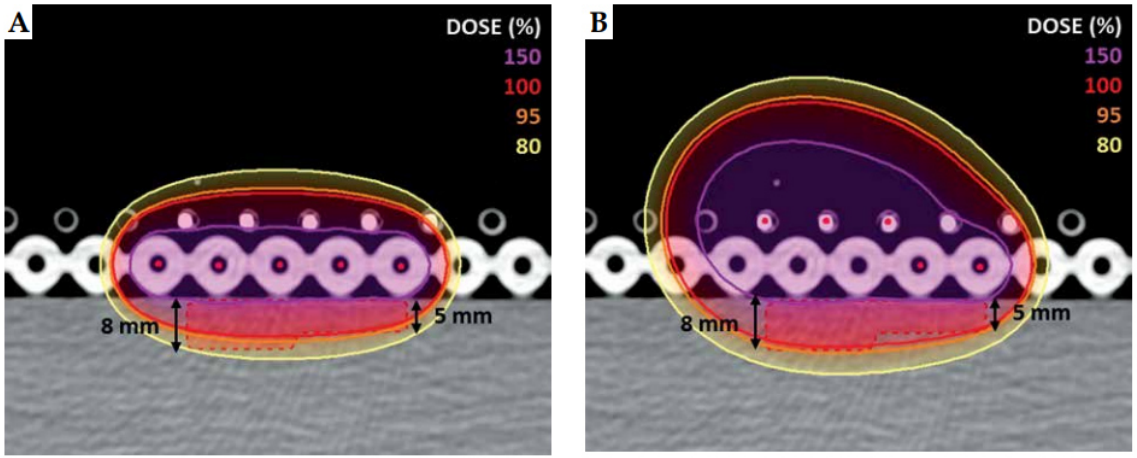

Fig. 1. Standard configuration of catheters (**A**) and multilayer configuration (**B**) calculated with the TG-43 formalism. 150%, 100%, 95%, and 80% isolines for the two configurations are compared. Treatment plans are optimized with 150% tangential to the skin, with a value of V_{150} (CTV) set to 1.5% for both the configurations

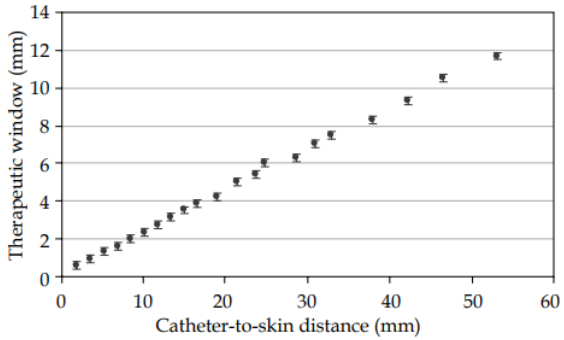

Fig. 2. Therapeutic window (TW) as a function of catheter-to-skin distance (mm) for a single active dwell position. TW increases in the depth, with values ranging from 0.6 to 11.7 mm for catheter-to-skin distances between 1.9 and 53.1 mm. Error bars show a 0.2 mm error for the distance measurement on TPS

BRACHYTHERAPY ALONE OR WITH NEOADJUVANT PHOTODYNAMIC THERAPY FOR AMELANOTIC CHOROIDAL MELANOMA

Functional Outcomes and Local Tumor Control

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Initial Treatment

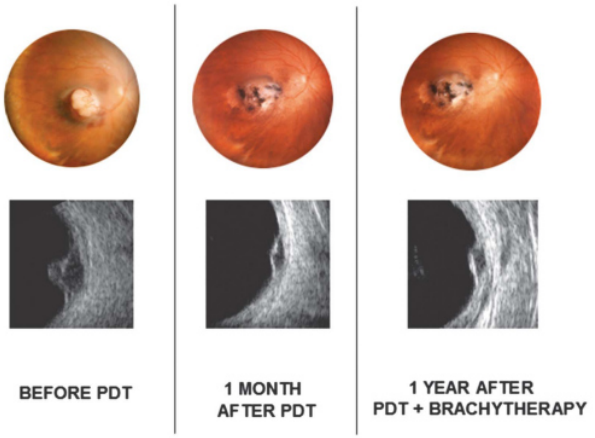

Fig. 2. Fundus photography and A-B scan ultrasonography of the same patient (patient n. 15, Group B) at diagnosis (left), 1 month after PDT (middle), and 1 year after PDT + brachytherapy (right).

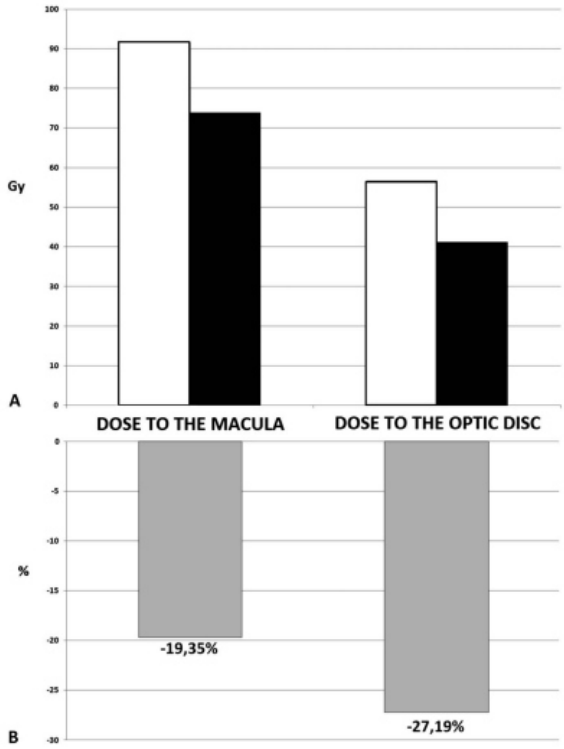

Fig. 1. Changes of the dose to the macula and optic disk before and after PDT (**A**) and percentage of dose reduction after PDT (**B**) in Group B1.

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ART
Advanced Radiation Therapy

Pictorial Essay

Original paper

Radiological and clinical findings in uveal melanoma treated by plaque interventional radiotherapy (brachytherapy): Visual atlas and literature review on response assessment

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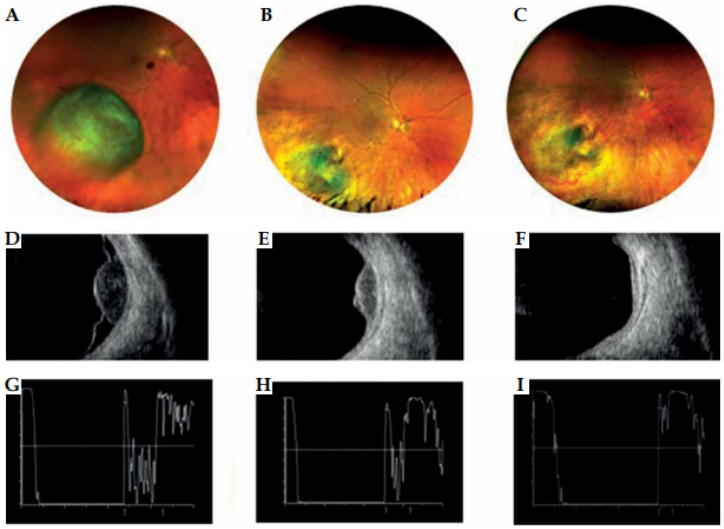
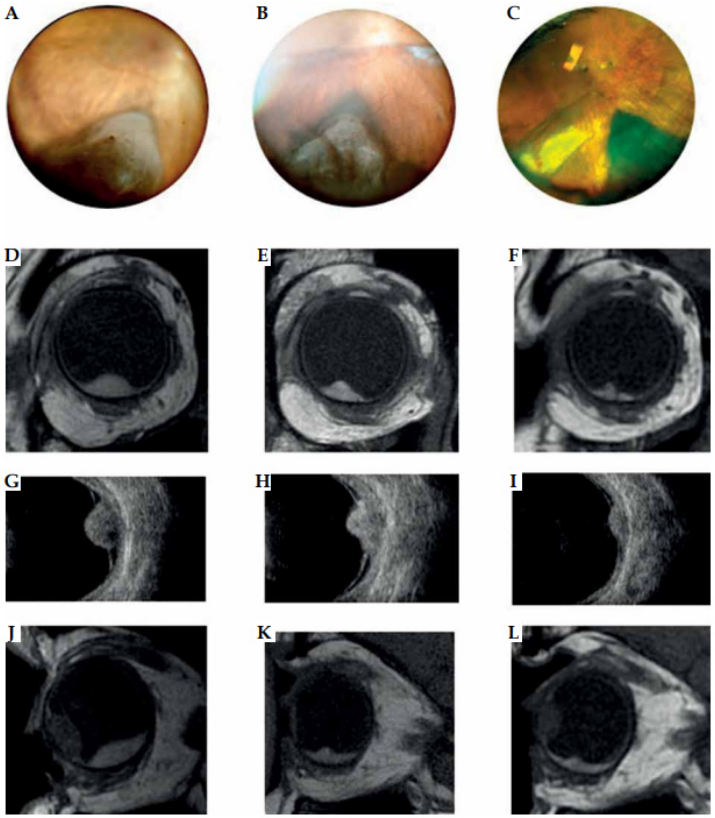


Imaging



Contact IRT

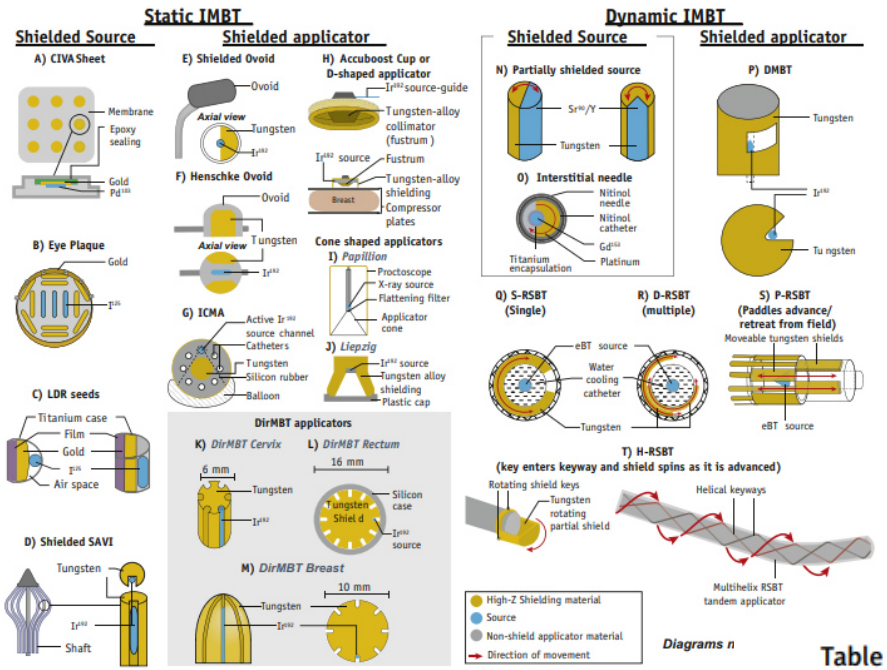


Table 1. Differences between static and dynamic intensity modulated interventional radiotherapy (IRT)

	Static IRT (eye plaque ^{125}I)	Dynamic IM-IRT (HDR/PDR)
Space	Size of plaque Shape of plaque Notches charged with seeds	Size of flap/mould Shape of flap/mould Active dwelling positions
Time	Only overall treatment duration may be chosen	Chance to vary independently each dwelling position activation time
Intensity	Activity of different seeds	Catheter-to-skin distance

HDR – high-dose-rate, PDR – pulsed-dose-rate

Callaghan CM et al. Systematic Review of Intensity-Modulated Brachytherapy (IMBT): Static and Dynamic Techniques. Int J Radiat Oncol Biol Phys. 2019

Primary site	Initial treatment	Imaging	IRT modality
Head and neck	RT +/- CT	MRI/CT/CT-PET	Interstitial/Contact
Skin (NMSC)	Hedgehog inhibitors/ (PD-L1) inhibitors	US	Contact
Eye	Photodynamic therapy	US/MRI	Contact

Thank you for your attention

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Gemelli ART (Advanced Radiation Therapy) - Interventional Oncology Center (IOC)

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