LA RADIOTERAPIA NEL CARCINOMA DEL CANALE ANALE:
INDICAZIONI E CRITERI GUIDA DI TRATTAMENTO

Rionero in Vulture, 31 ottobre 2014

Corso itinerante AIRO

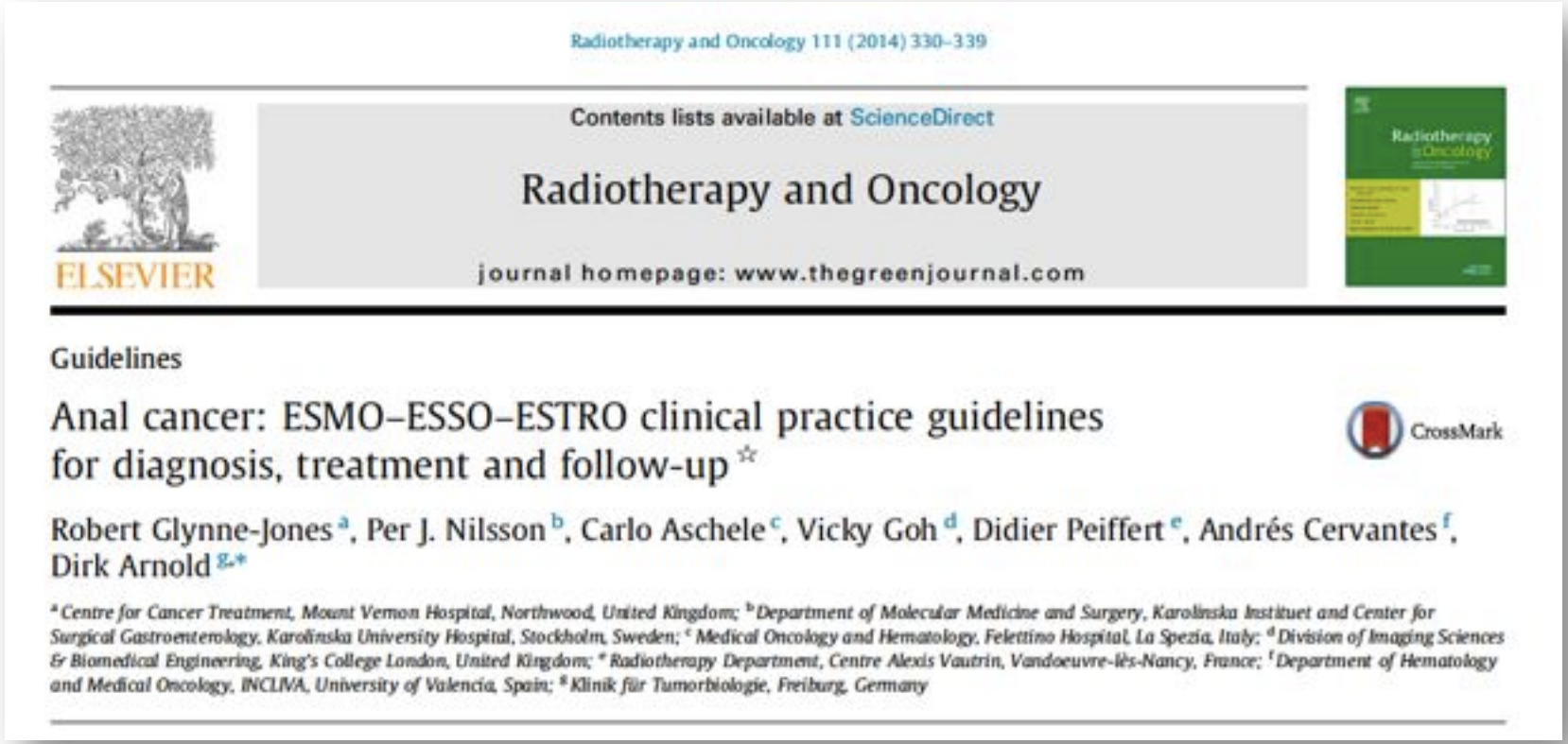
IL RUOLO DELLA BRACHITERAPIA

Luca TAGLIAFERRI

RADIOTERAPIA ONCOLOGICA - GEMELLI-ART

Policlinico Agostino Gemelli - Università Cattolica del Sacro Cuore - Roma

LINEE-GUIDA



Radiotherapy and Oncology 111 (2014) 330–339

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journal homepage: www.thegreenjournal.com

Guidelines

Anal cancer: ESMO–ESSO–ESTRO clinical practice guidelines for diagnosis, treatment and follow-up ☆

Robert Glynne-Jones [a], Per J. Nilsson [b], Carlo Aschele [c], Vicky Goh [d], Didier Peiffert [e], Andrés Cervantes [f], Dirk Arnold [g,*]

[a] Centre for Cancer Treatment, Mount Vernon Hospital, Northwood, United Kingdom; [b] Department of Molecular Medicine and Surgery, Karolinska Institutet and Center for Surgical Gastroenterology, Karolinska University Hospital, Stockholm, Sweden; [c] Medical Oncology and Hematology, Felettino Hospital, La Spezia, Italy; [d] Division of Imaging Sciences & Biomedical Engineering, King's College London, United Kingdom; [e] Radiotherapy Department, Centre Alexis Vautrin, Vandoeuvre-lès-Nancy, France; [f] Department of Hematology and Medical Oncology, INCLIVA, University of Valencia, Spain; [g] Klinik für Tumorbiologie, Freiburg, Germany

- Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, Arnold D. - Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. - **Radiother Oncol. 2014**

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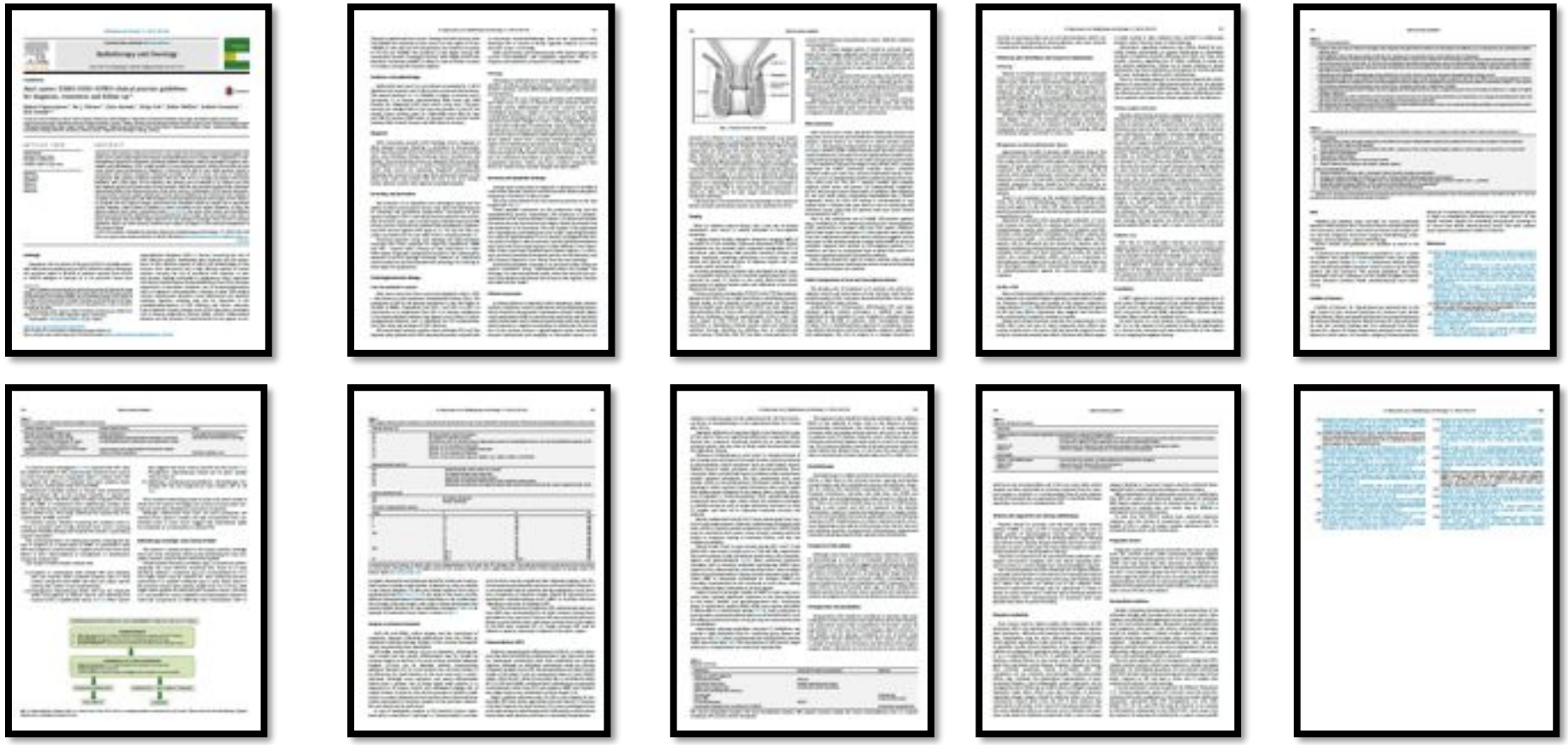

Gemelli ART
ADVANCED RADIATION THERAPY

- Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, Arnold D. - Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. - **Radiother Oncol. 2014**

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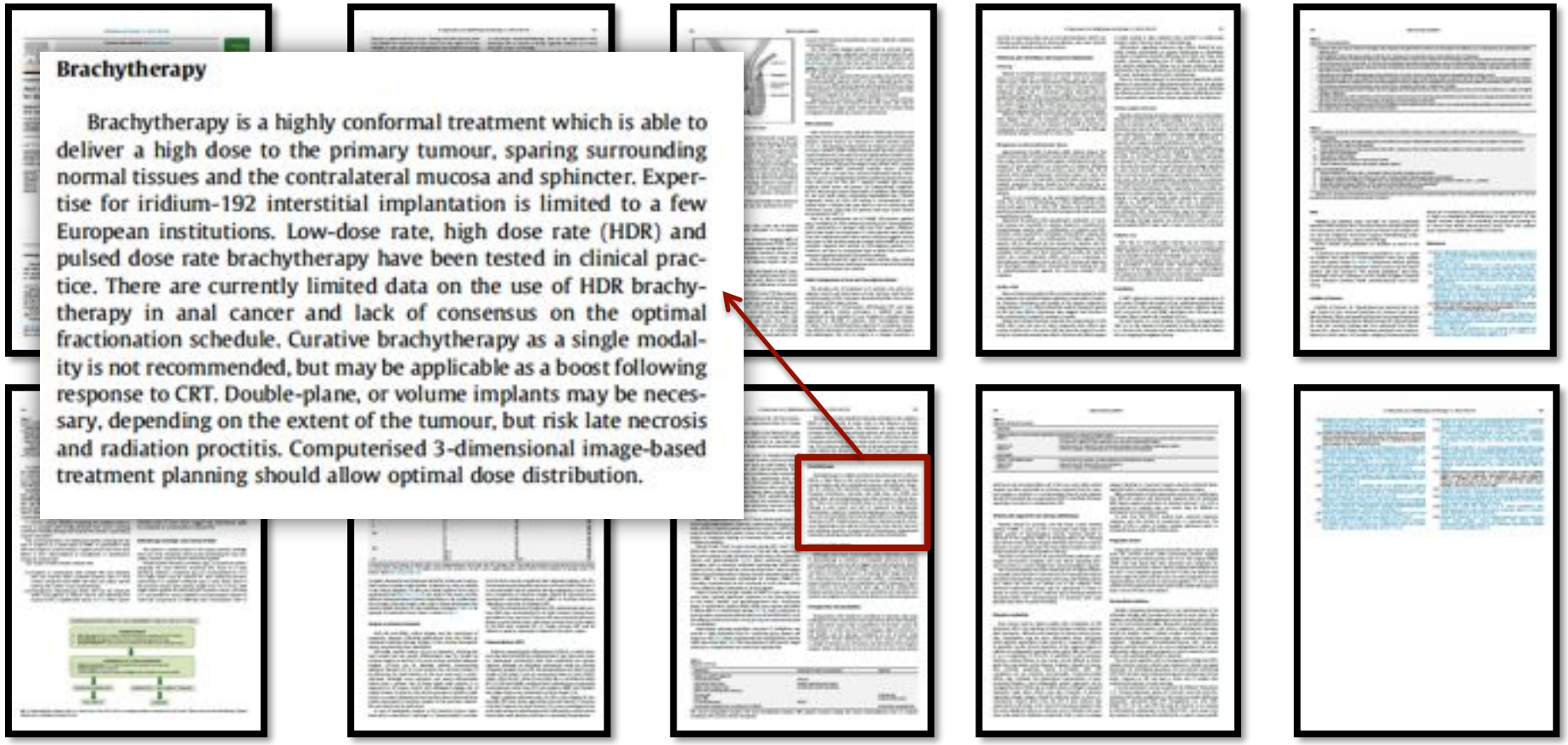

Brachytherapy

Brachytherapy is a highly conformal treatment which is able to deliver a high dose to the primary tumour, sparing surrounding normal tissues and the contralateral mucosa and sphincter. Expertise for iridium-192 interstitial implantation is limited to a few European institutions. Low-dose rate, high dose rate (HDR) and pulsed dose rate brachytherapy have been tested in clinical practice. There are currently limited data on the use of HDR brachytherapy in anal cancer and lack of consensus on the optimal fractionation schedule. Curative brachytherapy as a single modality is not recommended, but may be applicable as a boost following response to CRT. Double-plane, or volume implants may be necessary, depending on the extent of the tumour, but risk late necrosis and radiation proctitis. Computerised 3-dimensional image-based treatment planning should allow optimal dose distribution.

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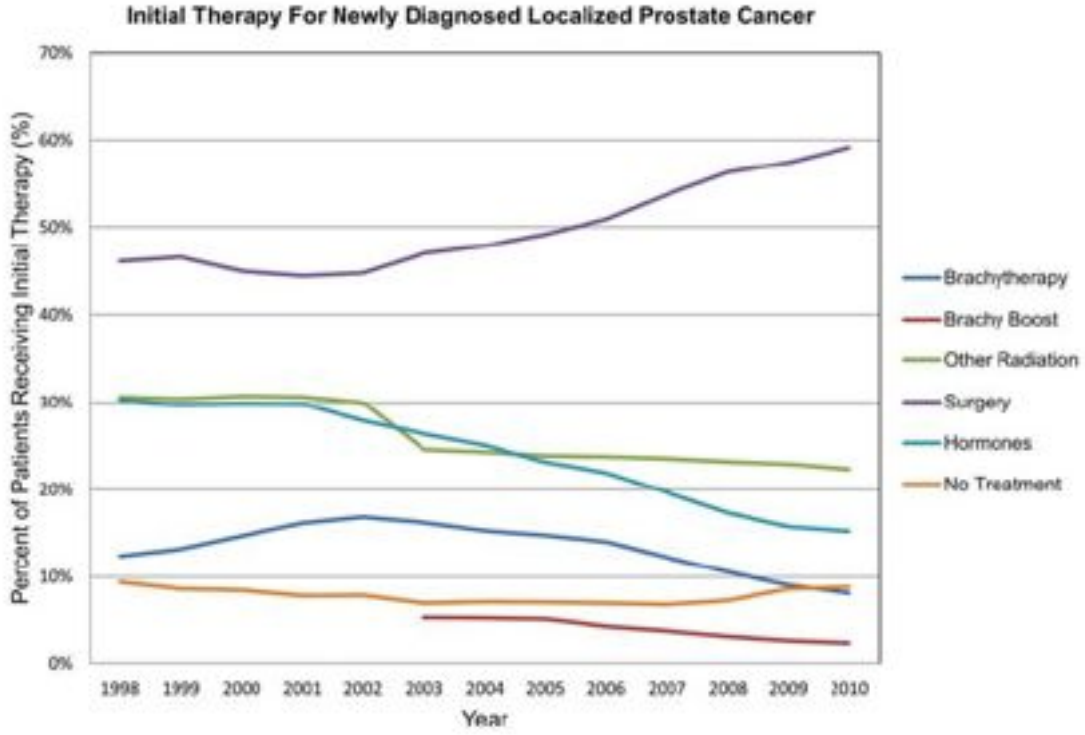
ADVANCED RADIATION THERAPY

- Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, Arnold D. - Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. - **Radiother Oncol. 2014**

The Rise and Fall of Prostate Brachytherapy: Use of Brachytherapy for the Treatment of Localized Prostate Cancer in the National Cancer Data Base

Jeffrey M. Martin, MD, MS[1]; Elizabeth A. Handorf, PhD[2]; Alexander Kutikov, MD[3]; Robert G. Uzzo, MD[3]; Justin E. Bekelman, MD[4]; Eric M. Horwitz, MD[1]; and Marc C. Smaldone, MD, MSHP[3]



Gemelli ART
ADVANCED RADIATION THERAPY

- Martin JM, Handorf EA, Kutikov A, Uzzo RG, Bekelman JE, Horwitz EM, Smaldone MC. The rise and fall of prostate brachytherapy: use of brachytherapy for the treatment of localized prostate cancer in the National Cancer Data Base. **Cancer. 2014**

Problematiche della BT

- Problematiche radio-protezionistiche
- Necessità di una sala operatoria/bunker dedicato
- Equipe specializzata in brachiterapia
- Rimborsi minori rispetto ad altre metodiche (es. IMRT)
- Costi maggiori
  - cateteri
  - sorgenti radioattive
  - gestione sala operatoria
- Degenza (impianto interstiziale)
- Rischio di sanguinamento/infezione

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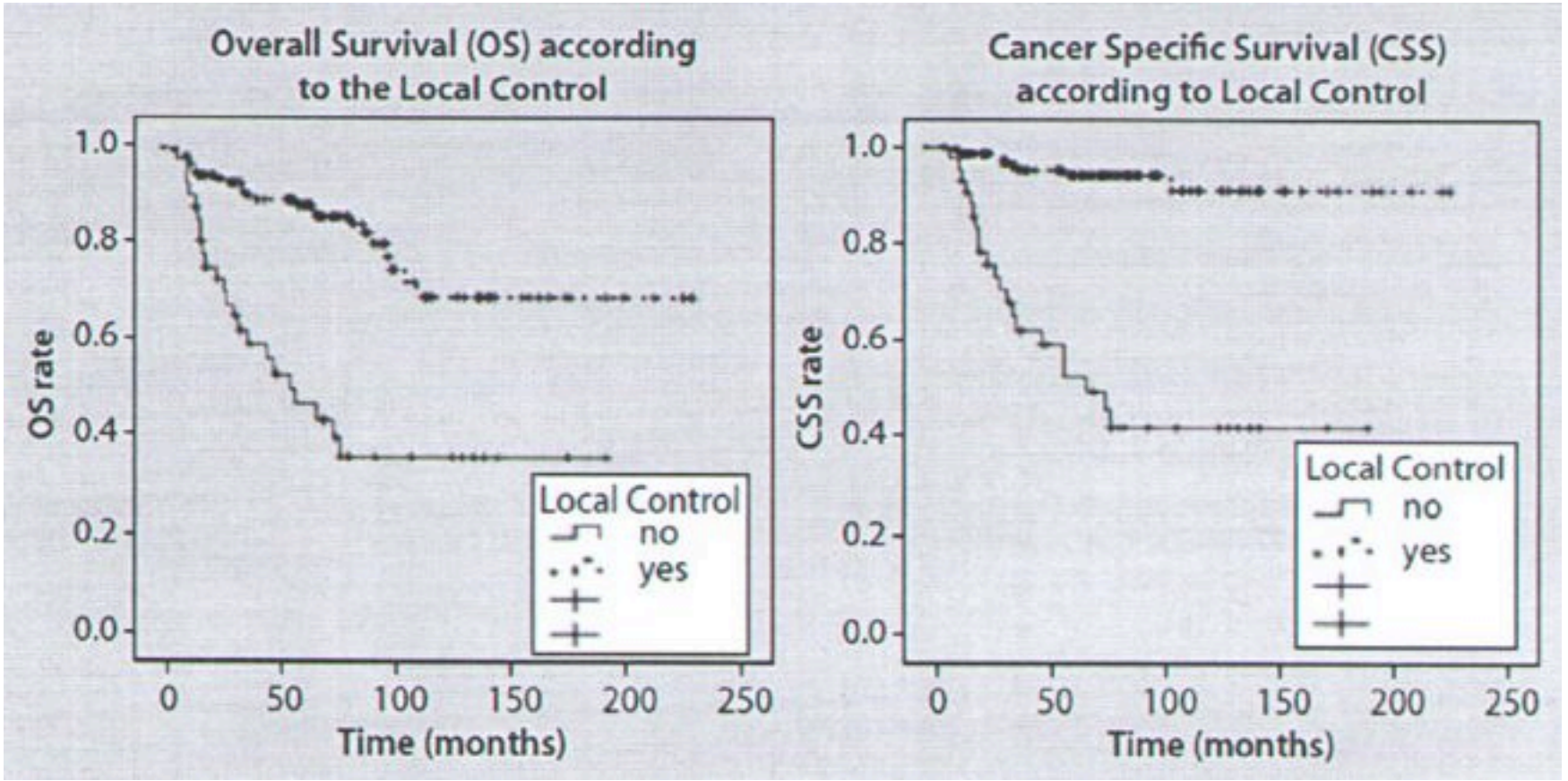
ADVANCED RADIATION THERAPY

Carcinoma del canale anale:
controllo locale e sopravvivenza



Gemelli ART
Advanced Radiation Therapy

- Lestrade L, De Bari B, Pommier P, Montbarbon X, Lavergne E, Ardiet JM, Carrie C. Role of brachytherapy in the treatment of cancers of the anal canal. Long-term follow-up and multivariate analysis of a large monocentric retrospective series. **Strahlenther Onkol. 2014**

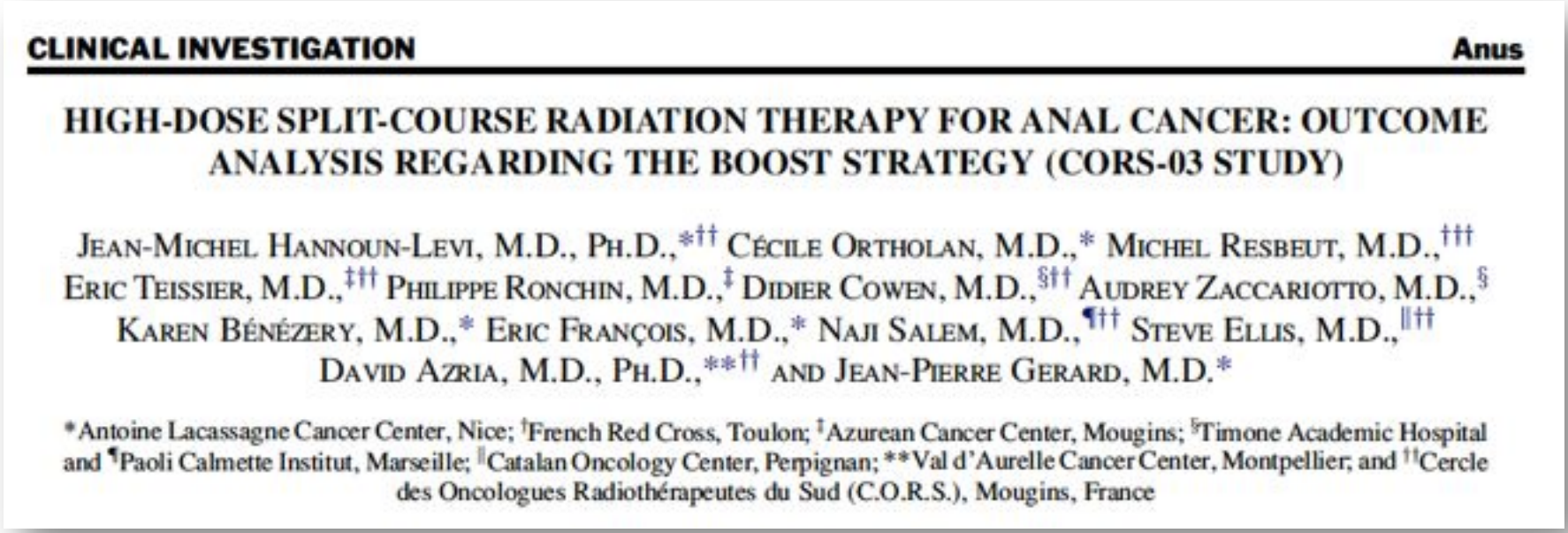
Vantaggi della BT

- Possibilità di prescrive una dose maggiore al target
- Possibilità di collimare la dose (IMBT)
- Minore dose agli organi a rischio (rapid fall off)
- Corto Overall Treatment Time (OTT)

Gemelli ART
Advanced Radiation Therapy

- Radiotherapy in Practice - Brachytherapy Peter Hoskin, Catherine Coyle
- Niehoff P, Kovács G. HDR brachytherapy for anal cancer. **J Gastrointest Oncol. 2014**

Boost: ERT o BT



CLINICAL INVESTIGATION Anus

HIGH-DOSE SPLIT-COURSE RADIATION THERAPY FOR ANAL CANCER: OUTCOME ANALYSIS REGARDING THE BOOST STRATEGY (CORS-03 STUDY)

JEAN-MICHEL HANNOUN-LEVI, M.D., PH.D.,*†† CÉCILE ORTHOLAN, M.D.,* MICHEL RESBEUT, M.D.,††† ERIC TEISSIER, M.D.,‡†† PHILIPPE RONCHIN, M.D.,‡ DIDIER COWEN, M.D.,§†† AUDREY ZACCARIOTTO, M.D.,§ KAREN BÉNÉZERY, M.D.,* ERIC FRANÇOIS, M.D.,* NAJI SALEM, M.D.,¶†† STEVE ELLIS, M.D.,‖†† DAVID AZRIA, M.D., PH.D.,**†† AND JEAN-PIERRE GERARD, M.D.*

*Antoine Lacassagne Cancer Center, Nice; †French Red Cross, Toulon; ‡Azurean Cancer Center, Mougins; §Timone Academic Hospital and ¶Paoli Calmette Institut, Marseille; ‖Catalan Oncology Center, Perpignan; **Val d'Aurelle Cancer Center, Montpellier; and ††Cercle des Oncologues Radiothérapeutes du Sud (C.O.R.S.), Mougins, France

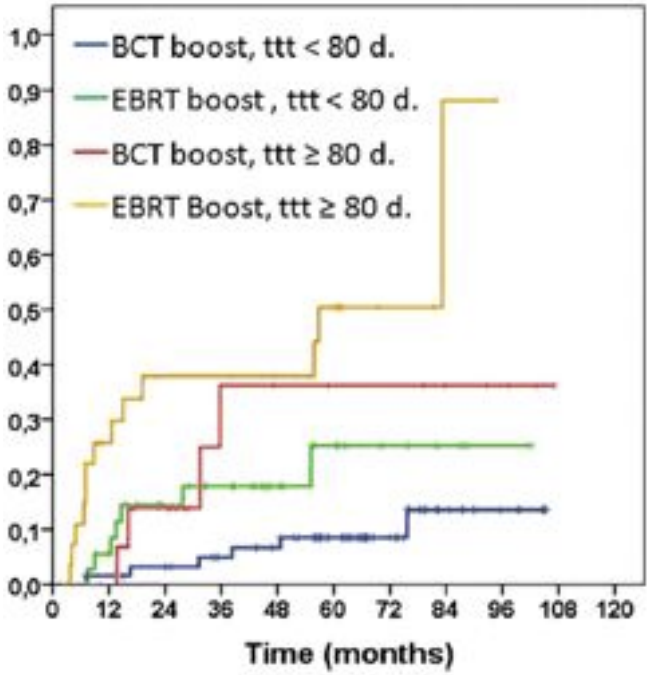
Gemelli ART ADVANCED RADIATION THERAPY

- Hannoun-Levi JM, Ortholan C, Resbeut M, Teissier E, Ronchin P, Cowen D, Zaccariotto A, Bénézery K, François E, Salem N, Ellis S, Azria D, Gerard JP. High-dose split-course radiation therapy for anal cancer: outcome analysis regarding the boost strategy (CORS-03 study). **Int J Radiat Oncol Biol Phys. 2011**

Boost: ERT o BT

		5-year OS		5-year CRLR		5-year CFS	
Factors	Categories	%	*p* value	%	*p* value	%	*p* value
Gender	Male	67	0.16	21	0.95	67	0.60
	Female	82		20		82	
Age	< 67 years	82	0.32	27	0.22	70	0.13
	≥ 67 years	75		25		60	
T stage	T1–2	84	0.009	15	0.03	72	0.04
	T3–4	68		36		51	
Nodal status	N0–1	83	<0.001	19	0.07	72	0.02
	N2–3	45		28		46	
Boost technique	BCT	78	0.47	12	0.002	71	0.04
	EBRT	80	–	33		56	
OTT	< 80	84	<0.001	14	0.005	74	0.004
	≥ 80	67		34		50	

Abbreviations: OS = overall free survival; CRLR = cumulated rate of local recurrence; CFS = colostomy-free survival; OTT = overall treatment time.



Conclusion: In anal cancer, when OTT is <80 days, BCT boost is superior to EBRT boost for CRLR. These results suggest investigating the benefit of BCT boost in prospective trials. © 2010 Elsevier Inc.

Gemelli ART
ADVANCED RADIATION THERAPY

- Hannoun-Levi JM, Ortholan C, Resbeut M, Teissier E, Ronchin P, Cowen D, Zaccariotto A, Bénézery K, François E, Salem N, Ellis S, Azria D, Gerard JP. High-dose split-course radiation therapy for anal cancer: outcome analysis regarding the boost strategy (CORS-03 study). **Int J Radiat Oncol Biol Phys. 2011**

Boost: ERT o BT

International Journal of Radiation Oncology biology • physics

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Clinical Investigation: Gastrointestinal Cancer

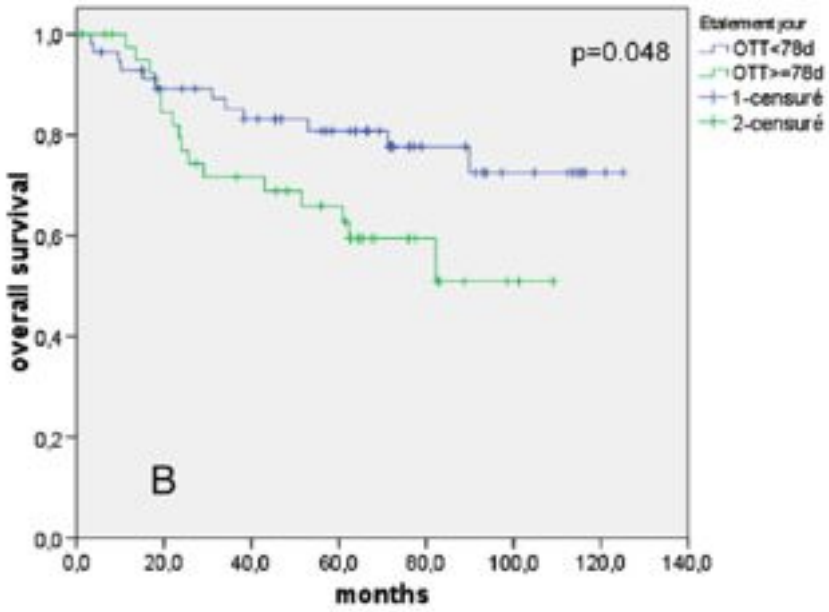
Role of Brachytherapy in the Boost Management of Anal Carcinoma With Node Involvement (CORS-03 Study)

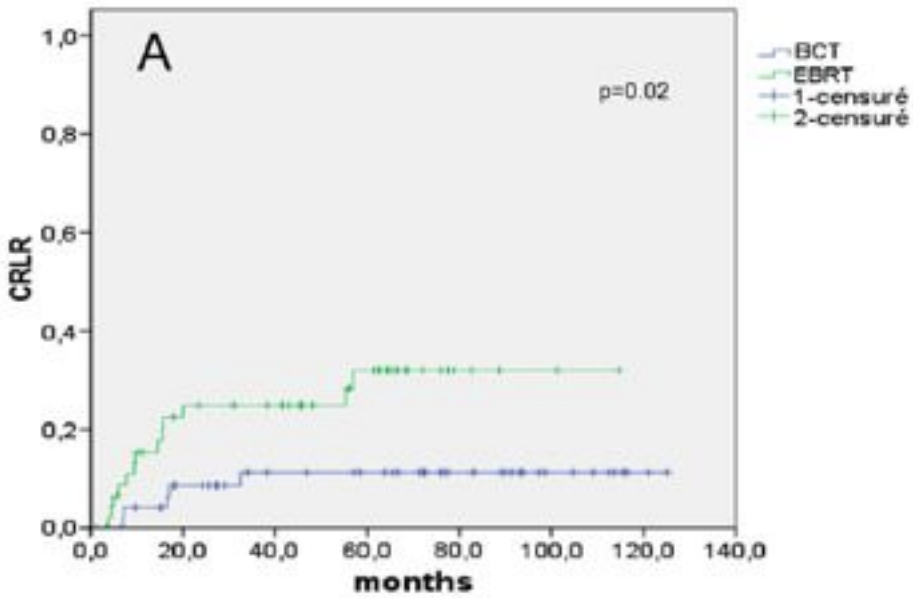
Laurence Moureau-Zabotto, MD,* Cecile Ortholan, MD, PhD,† Jean-Michel Hannoun-Levi, MD, PhD,‡ Eric Teissier, MD,§ Didier Cowen, MD, PhD,‖,¶ Nagi Salem, MD,* Claire Lemanski, MD,# Steve Ellis, MD,** and Michel Resbeut, MD*,**

Gemelli ART Advanced Radiation Therapy

- Moureau-Zabotto L, Ortholan C, Hannoun-Levi JM, Teissier E, Cowen D, Salem N, Lemanski C, Ellis S, Resbeut M. Role of brachytherapy in the boost management of anal carcinoma with node involvement (CORS-03 study) **- Int J Radiat Oncol Biol Phys. 2013**

Boost: ERT o BT



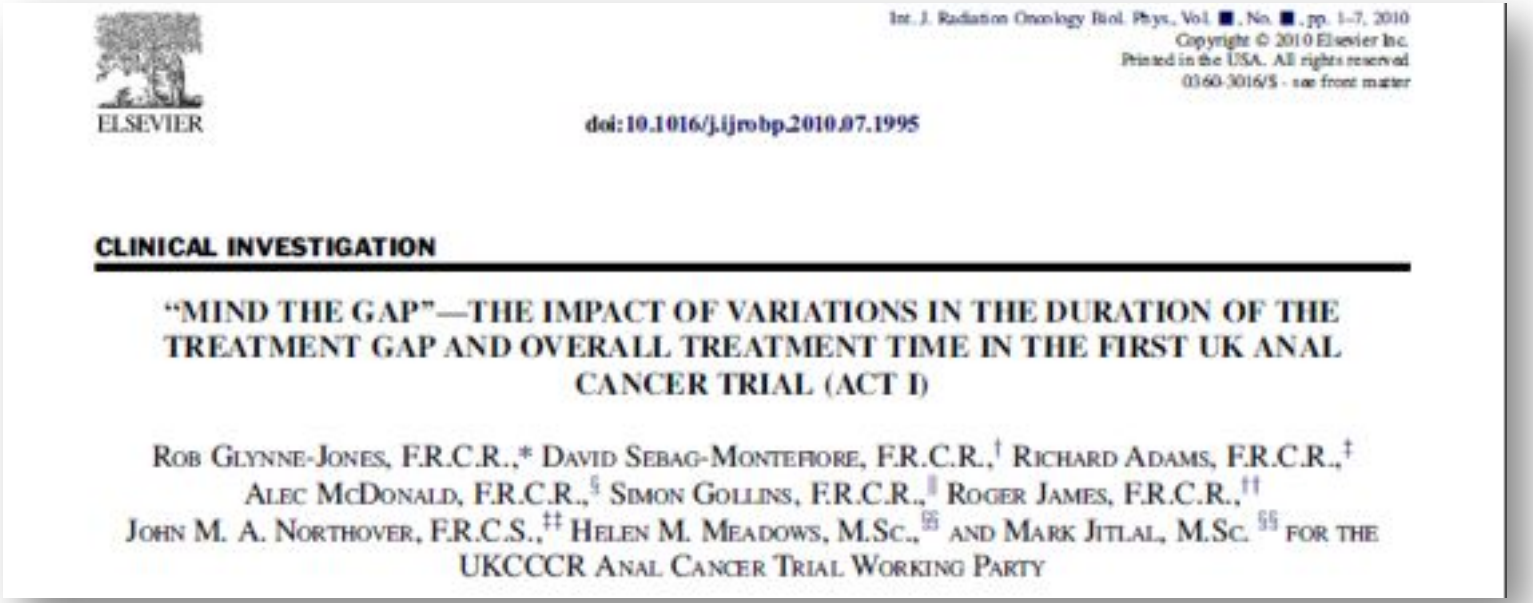


Conclusion: In anal cancer, even in the case of initial perirectal node invasion, BCT boost is superior to EBRT boost for CRLR, without an influence on OS, suggesting that N1 status should not be a contraindication to use of a BCT boost technique, as well as emphasizing the important of investigating the benefit of BCT boost in prospective randomized trials. © 2013 Elsevier Inc.

Gemelli ART
Advanced Radiation Therapy

- Moureau-Zabotto L, Ortholan C, Hannoun-Levi JM, Teissier E, Cowen D, Salem N, Lemanski C, Ellis S, Resbeut M. Role of brachytherapy in the boost management of anal carcinoma with node involvement (CORS-03 study) **- Int J Radiat Oncol Biol Phys. 2013**

Boost ERT o BT: Tossicità



Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–7, 2010
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ELSEVIER

doi:10.1016/j.ijrobp.2010.07.1995

CLINICAL INVESTIGATION

"MIND THE GAP"—THE IMPACT OF VARIATIONS IN THE DURATION OF THE TREATMENT GAP AND OVERALL TREATMENT TIME IN THE FIRST UK ANAL CANCER TRIAL (ACT I)

ROB GLYNNE-JONES, F.R.C.R.,* DAVID SEBAG-MONTEFIORE, F.R.C.R.,† RICHARD ADAMS, F.R.C.R.,‡ ALEC MCDONALD, F.R.C.R.,§ SIMON GOLLINS, F.R.C.R.,‖ ROGER JAMES, F.R.C.R.,†† JOHN M. A. NORTHOVER, F.R.C.S.,‡‡ HELEN M. MEADOWS, M.SC.,§§ AND MARK JITLAL, M.SC.§§ FOR THE UKCCCR ANAL CANCER TRIAL WORKING PARTY

Conclusions: These results question the benefit of a radiotherapy boost after a 6-week gap. The higher doses of a boost may contribute more to an increased risk of late morbidity, rather than local control. © 2010 Elsevier Inc.

Gemelli ART
ADVANCED RADIATION THERAPY

- Glynne-Jones R, Sebag-Montefiore D, Adams R, McDonald A, Gollins S, James R, Northover JM, Meadows HM, Jitlal M; "Mind the gap"--the impact of variations in the duration of the treatment gap and overall treatment time in the first UK Anal Cancer Trial (ACT I). **Int J Radiat Oncol Biol Phys. 2011**

Boost ERT o BT: Tossicità

577 pazienti - boost dopo 6 settimane: EBRT (15 Gy) or iridium-192 implant (25 Gy)

ULCERA/RADIONECROSI

BOOST	NO BOOST	
8%	0%	p=0.03

ULCERA/RADIONECROSI

BT BOOST	ERT BOOST	
14%	6%	p=0.003

Gemelli ART
ADVANCED RADIATION THERAPY

- Glynne-Jones R, Sebag-Montefiore D, Adams R, McDonald A, Gollins S, James R, Northover JM, Meadows HM, Jitlal M; "Mind the gap"--the impact of variations in the duration of the treatment gap and overall treatment time in the first UK Anal Cancer Trial (ACT I). **Int J Radiat Oncol Biol Phys. 2011**

Brachiterapia LDR

- **Papillion et al.**
  - *221 pazienti*
  - *RT/CT (5-Fu + MMC) ➔ BT-LDR (15-20Gy)*
  - *5-years LC: 61% - 5-years SVV: 65%*
  - *Funzione anale conservata: 90%*

- **Berger et al.**
  - *69 pazienti*
  - *RT o RT/TC (5-Fu + MMC) (40Gy) ➔ BT-LDR (20Gy)*
  - *5-years LC: 59%*
  - *5-Years Colostomy rate: 33%*

Gemelli ART
ADVANCED RADIATION THERAPY

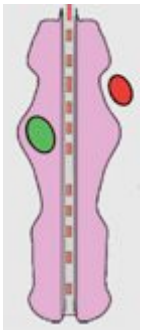
- Vordermark D, Flentje M, Sailer M, et al. Intracavitary afterloading boost in anal canal carcinoma. Results, function and quality of life. **Strahlenther Onkol 2001**
- Papillon J, Montbarbon JF, Gerard JP, et al. Interstitial curietherapy in the conservative treatment of anal and rectal cancers. **Int J Radiat Oncol Biol Phys 1989**
- Berger C, Félix-Faure C, Chauvet B, et al. Conservative treatment of anal canal carcinoma with external radiotherapy and interstitial brachytherapy, with or without chemotherapy: long-term results. **Cancer Radiother 1999**

Moderna Brachiterapia

IMBT
Intensity Modulated
BrachyTherapy

IGBT
Image Guided
BrachyTherapy

ABT
Adapted
BrachyTherapy



IABT

Image Adapted
BrachyTherapy

Gemelli
ADVANCED RADIATION THERAPY

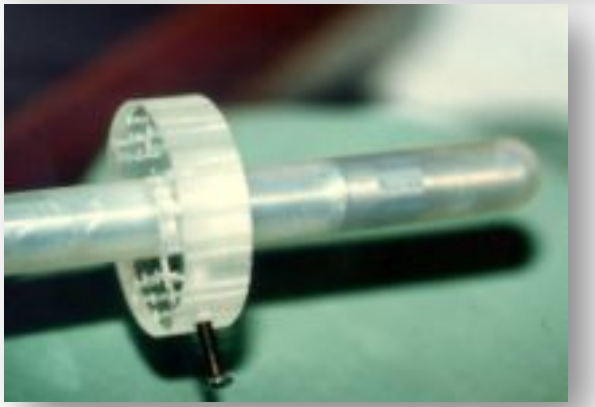
- Meyer JE, Brocks C, Maune S, Strnad V, Werner JA, Wollenberg B, Kovács G - Brachytherapy for the treatment of head and neck cancer. **HNO. 2010 Sep;58(9):947-58.**

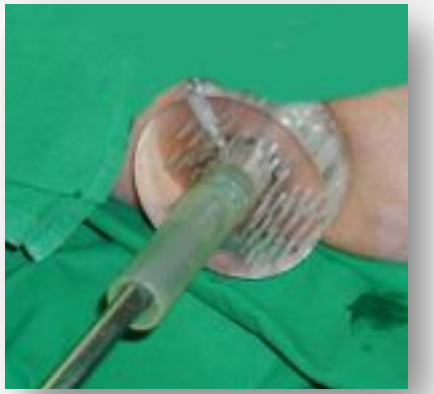
US guided-BT

Multimodal therapy of anal cancer added by new endosonographic-guided brachytherapy

J. M. Doniec,[1]* B. Schniewind,[1]* G. Kovács,[2] V. Kahlke,[1] M. Loehnert,[3] B. Kremer[1]

[1] Clinic for General and Thoracic Surgery, University Clinic of Schleswig-Holstein, Campus Kiel, Arnold-Heller-Strasse 7, 24105 Kiel, Germany
[2] Interdisciplinary Center of Brachytherapy and Clinic of Radiation Therapy, University Clinic of Schleswig-Holstein, Campus Kiel, Arnold-Heller-Strasse 7, 24105 Kiel, Germany
[3] Städtisches Klinikum Bielefeld Rosenhöhe, An der Rosenhöhe 27, 33647 Bielefeld, Germany





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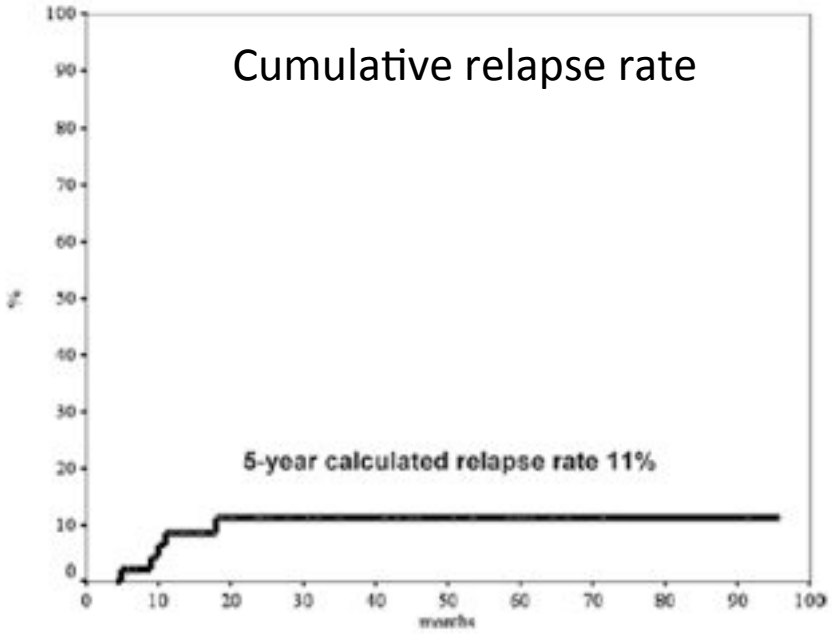
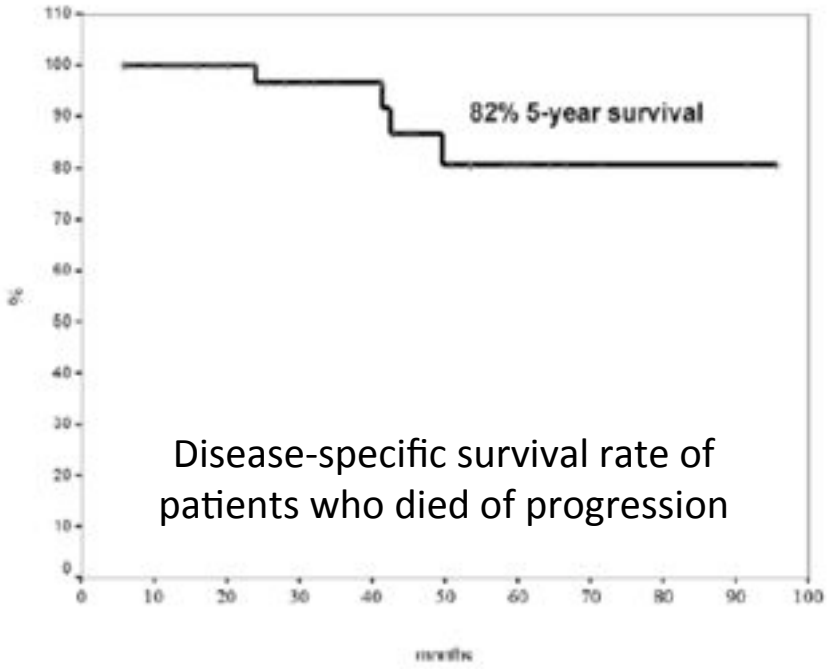
ADVANCED RADIATION THERAPY

- Doniec JM, Schniewind B, Kovács G, Kahlke V, Loehnert M, Kremer B. - Multimodal therapy of anal cancer added by new endosonographic-guided brachytherapy**. Surg Endosc. 2006**

US guided-BT





no stenosi anali o rettali – 6% incontinenza anale

- Doniec JM, Schniewind B, Kovács G, Kahlke V, Loehnert M, Kremer B. - Multimodal therapy of anal cancer added by new endosonographic-guided brachytherapy. **Surg Endosc. 2006**

US guided-BT

IMAGE GUIDED BRACHYTHERAPY

+

STEPPING SOURCE

IMPROVE LOCAL CONTROL

AND MINIMIZE MORBIDITY

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ADVANCED RADIATION THERAPY

- Doniec JM, Schniewind B, Kovács G, Kahlke V, Loehnert M, Kremer B. - Multimodal therapy of anal cancer added by new endosonographic-guided brachytherapy**. Surg Endosc. 2006**

MRI vs US

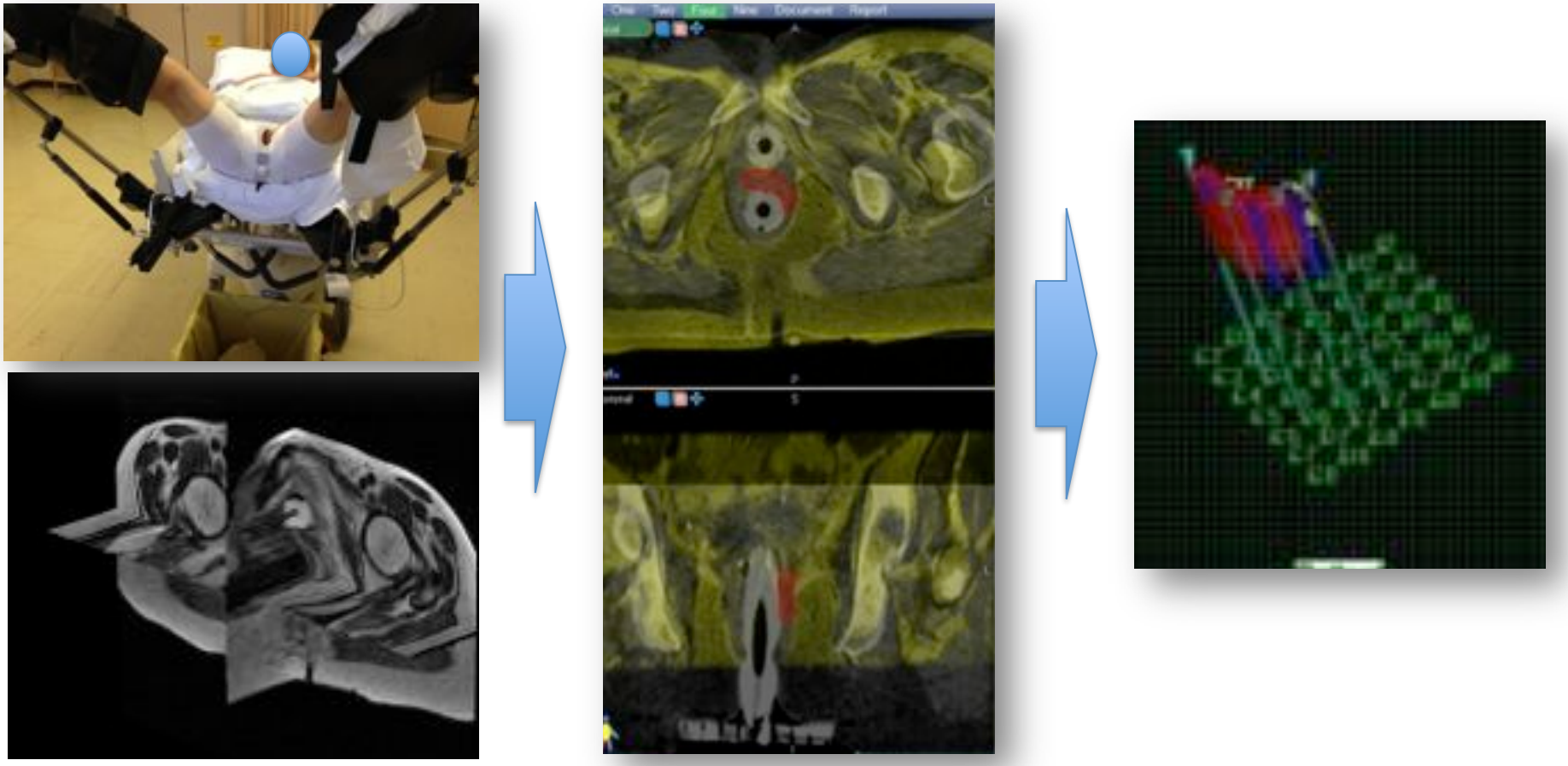
MRI offre maggiori informazioni:

- Contrasto e risoluzione spaziale
- dimensioni del tumore
- estensione e l'infiltrazione locale
- l'invasione di organi adiacenti
- Impianto multi-planare

Gemelli ART
Advanced Radiation Therapy

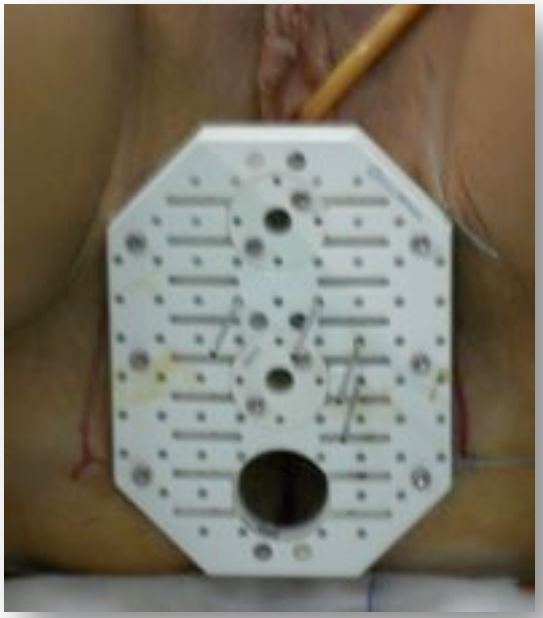
- Goh V, Gollub FK, Liaw J, et al. Magnetic resonance imaging assessment of squamous cell carcinoma of the anal canal before and after chemoradiation: can MRI predict for eventual clinical outcome? **Int J Radiat Oncol Biol Phys 2010**
- Glynne-Jones R, Nilsson PJ, Aschele C, Goh V, Peiffert D, Cervantes A, Arnold D. - Anal cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. - **Radiother Oncol. 2014**

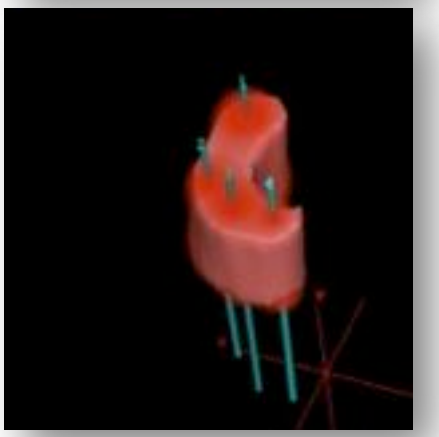
MR-guided BT



- La brachiterapia RM-guidata (RM-GBT) nel tumore del canale anale: studio preliminare dosimetrico e clinico - L. Tagliaferri, S. Manfrida, G.C. Mattiucci, M.M. Colangione, V. Masiello, S. Luzi, D. Smaniotto, B. Barbaro, A. Larghi, V. Valentini – Università Cattolica S. C. – Roma - **Congresso AIRO 2013**

MR-guided BT





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MR-guided BT

- Da 2/2012 a 7/2014: 9 pz
- Tutti i pz hanno effettuato la BT come boost dopo RT/CT
- Nessuna complicazione durante la procedura
- Buona compliance del paziente alla procedura
- La percentuale media di CTV coperta da meno del 100% della dose è stata del 4,9%

Gemelli ART
ADVANCED RADIATION THERAPY

- La brachiterapia RM-guidata (RM-GBT) nel tumore del canale anale: studio preliminare dosimetrico e clinico - L. Tagliaferri, S. Manfrida, G.C. Mattiucci, M.M. Colangione, V. Masiello, S. Luzi, D. Smaniotto, B. Barbaro, A. Larghi, V. Valentini – Università Cattolica S. C. – Roma - **Congresso AIRO 2013**

Prescrizione

LDR or PDR

- Sola BT: 60Gy at 0.5 Gy/h
- Boost BT (CT) EBRT (45-50Gy): 15-30 Gy at 0.5Gy/h

HDR

- Sola BT: 30-36Gy in 5-6 fx
- Boost BT (CT) EBRT (45-50Gy): 8-16.5 Gy in 2-3 fx

Gemelli ART
ADVANCED RADIATION THERAPY

- Radiotherapy in Practice - Brachytherapy Peter Hoskin, Catherine Coyle
- The GEC ESTRO Handbook of Brachytherapy
- Niehoff P, Kovács G. HDR brachytherapy for anal cancer. **J Gastrointest Oncol. 2014**

Controindicazioni

- *Tumore supera la metà della circonferenza*
- *Tumore supera 10 mm di spessore*
- *Tumore supera 5 cm di lunghezza cranio-caudale*
- *Controindicazioni all'anestesia*

Gemelli ART
Advanced Radiation Therapy

- Radiotherapy in Practice - Brachytherapy Peter Hoskin, Catherine Coyle
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Conclusioni

- Nel carcinoma del canale anale il controllo locale è correlato con una maggiore sopravvivenza e con una maggiore qualità di vita (assenza di colostomia)

- La brachiterapia può essere presa in considerazione per un dose-escalation al fine di aumentare il controllo locale

- Un minor OTT migliora i risultati clinici.

Conclusioni

- La BT determina una maggiore tossicità locale rispetto alla ERT (ulcera necrotica) ma IABT migliora il controllo locale e riduce la tossicità rispetto all'uso delle "sorgenti lineari"

- La BT interstiziale è equipe dipendente (Radioterapista-Fisico-Infermiere) per questo motivo dovrebbe essere eseguita in centri con un elevato numero di casi

UN BOOST BT È RACCOMANDATO SE NON VI SONO CONTROINDICAZIONI E SE IL PAZIENTE È TRATTATO IN UN CENTRO CON ESPERIENZA IN IABT, SOPRATTUTTO IN PRESENZA DI UNA SCARSA RISPOSTA AL TRATTAMENTO

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