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- Definition and background
- Conditioning Factors
- New Technologies
- Intervention strategies

Definition and background

Conditioning Factors

- New Technologies
- Intervention strategies

Definition of compliance

- In Physics: a coefficient expressing the responsiveness of a mechanical system to a periodic force
- The act or process of doing what you have been asked or **ordered** to do
- Adhering to a rule, such as a policy, standard, specification, or law.
- The act of conforming, acquiescing, or yielding
- The ability to meet halfway



Metrics for Compliance

In Oncological Treatment

In Radiation Treatment

ADHERENCE to treatment

RT dose n° of CT cycles CT dose reduction

TIME

Days of interruptions

Treatments **delays**

Overall treatment time





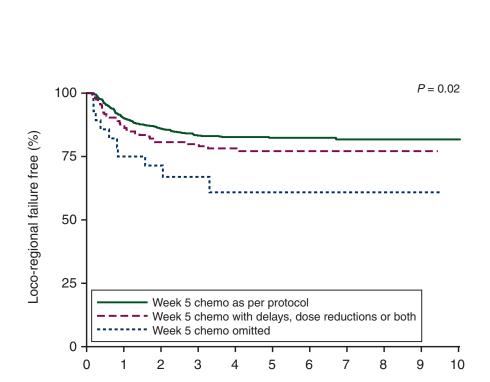
ORIGINAL ARTICLE

Α

Impact of compliance to chemoradiation on long-term outcomes in squamous cell carcinoma of the anus: results of a *post hoc* analysis from the randomised phase III ACT II trial $\stackrel{\mathcal{k}}{\sim}$

R. Glynne-Jones^{1*}, H. M. Meadows², A. Lopes², R. Muirhead³, D. Sebag-Montefiore⁴ & R. Adams⁵, on behalf of the ACTII study group

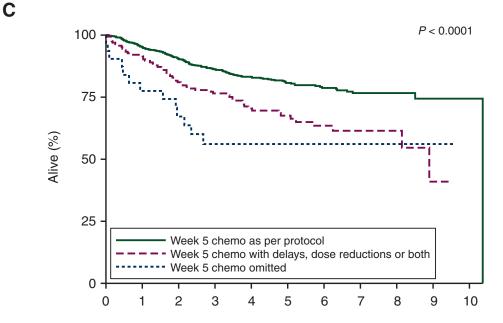
¹Mount Vernon Centre for Cancer Treatment, Mount Vernon Hospital, Northwood; ²Cancer Research UK & University College London Cancer Trials Centre, UCL, London; ³Oxford Cancer & Haematology Centre, Oxford University Hospitals, Oxford; ⁴University of Leeds, Leeds Cancer Centre, Leeds; ⁵School of Medicine, Cardiff University, Cardiff, UK



Time since 7 weeks post randomisation (years)

anal CANCER

In Oncological Treatment



Time since 7 weeks post randomisation (years)





С

ORIGINAL ARTICLE

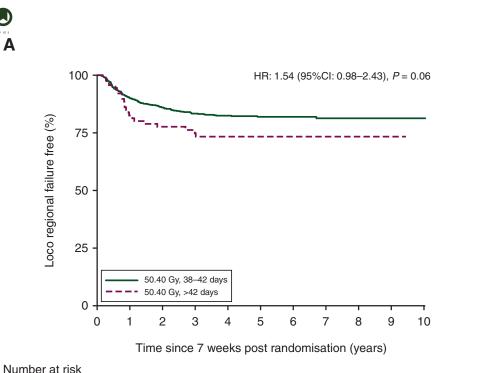
UP AT S

Α

Impact of compliance to chemoradiation on long-term outcomes in squamous cell carcinoma of the anus: results of a post hoc analysis from the randomised phase III ACT II trial $\stackrel{\mbox{\tiny\sc black}}{\longrightarrow}$

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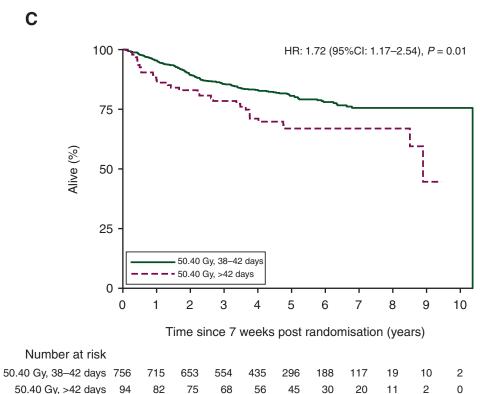
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40 Gy, 38–42 days	756	640	580	492	386	261	173	108	46	9	1	
50.40 Gy, >42 days	94	68	59	52	45	38	24	16	10	2	0	

In Radiation Treatment

anal CANCER



Time and outcomes

TUMOR DOSE VOLUME **TIME**

$$EQD2 = D\left(\frac{d+\alpha/\beta}{2+\alpha/\beta}\right) - D_{prolif}\left(T - T_{k}\right)$$

- T_k Day (from start) when proliferation begins
- T Days, overall treatment time
- D_{prolif} EQD2 per day lost to proliferation. Only if $T \ge T_k$, otherwise zero

D_{prolif} reduces effective dose

ESTR02021

Reminder:

 D_{prolif}



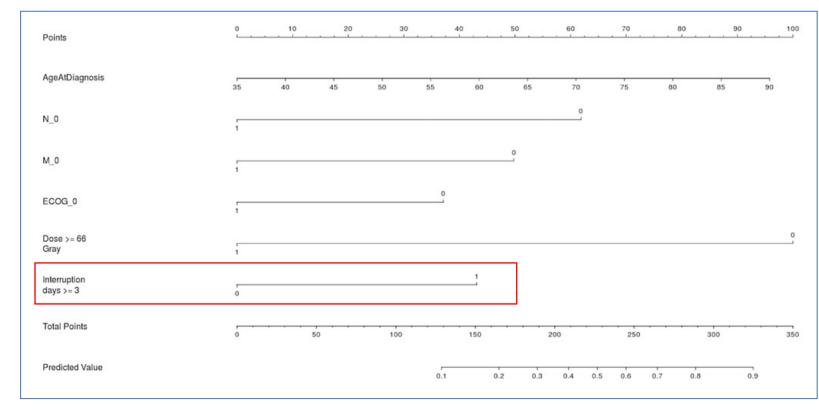
The role of TIME in outcomes predicion

The development of overall survival in oropharingeal cancer:

PRO.ME.THEO 2 years OS nomogram

AGE DOSE PS TIME COMPLIANCE

174 (79.8%) were analyzed.interruption were consideredPMs were developed and represented by nomograms



Miccichè F et al. Acta Otholaryng Italica 2021

The role of TIME in outcomes predicion

AgeAtDiagnosis	N 0	ECOG 0	Dose >= 66 Gray	Interruption days >= 3 death_risk_2y (%)	Risk Categories
	65 N-	Si	Si	No	2
	65 N-	No	No	No	3 Very Good
	75 N-	Si	Si	No	
	65 N-	No	SI	No	4
	65 N-	Si	Si	SI	OSS > 90 % at 2 y
	75 N-	No	Si	No	$_{6}$ 033 $>$ 30 /0 dt 2 y
	65 N+	Si	Si	No	7
	75 N-	Si	Si	SI	<mark>7</mark>
	65 N-	No	SI	SI	1
	75 N+	Si	Si	No	1
	75 N-	No	Si	SI	15
	65 N +	No	Si		Good
	65 N-	Si	No	No	
	65 N+	Si	Si	SI 1	17
	75 N+	No	Si	No	OSS > 75-85 % at 2 y
	75 N-	Si	No	No 2	033 ~ 73-03 /0 at Z y
	75 N+	Si	Si		24
	65 N+	No	Si	SI	33
	65 N-	Si	No	SI	33
	75 N-	No	No		Bad
	75 N+	No	Si	SI 4	
	75 N-	Si	No	SI 4	
	65 N+	Si	No		OSS > 50-70 % at 2 y
	65 N-	No	No	SI	
	75 N+	Si	No	No 5	53
	65 N+	No	No		53
	75 N-	No	No	SI	Very Bad
	65 N+	Si	No		
	75 N+	No	No		72
	75 N+	Si	No	SI	OSS > 15-40 % at 2 y
	65 N+	No	No	SI	32 033 > 13-40 /0 dl Z y
	75 N+	No	No	SI	37

Miccichè F et al. Acta Otholaryng Italica 2021

H&N CANCER

Definition and background

- Conditioning Factors
- New Technologies
- Intervention strategies

Factors affecting compliance

- 1. TREATMENTS
- 2. COMORBIDITIES
- 3. SOCIO-ECONOMICS
- 4. PERSONAL Sphere

rectal CANCER

1. Treatment Intensity

oxaliplatin randomized trials	-	Number of	pCR	D	FS
	oxaliplatin	patients		diff	р
	ACCORD 12	584	X	4.3%	0.25
	NSABP R04	1284	X	5%	0.34
	STAR 01	739	X	3.6%	0.37
	CAO-ARO-AIO 04	1236	1	4.7%	0.03
	CHINESE	206	X	10.6%	0.08
	PETACC-6	1094 X Full par pendir		-	
	FORWARK	475	1	Follow-u continue	-

rectal CANCER

1. Treatment Intensity

oxaliplatin randomized trials	Neoadjuvant	Number of	pCR	D	FS	Acute	compliance
	oxaliplatin	patients		diff	р	toxicity	
	ACCORD 12	584	Х	4.3%	0.25	1	V
	NSABP R04	1284	Х	5%	0.34	1	Ļ
	STAR 01	739	Х	3.6%	0.37	1	Ļ
	CAO-ARO-AIO 04	1236	1	4.7%	0.03	=	=*
*% of Adherence to RT	CHINESE	206	Х	10.6%	0.08	1	V
% of Adherence to standard RTCT (only 5FU)	PETACC-6	1094	X		paper Iding	1	Ļ
Lower oxaliplatin dose/cycles compared to other trials	FORWARK	475	1	Follow-u continue	-	1	=

H&N CANCER

1. Radiotherapy Quality

TROG 02.02 RCT RT + CIS vs RT CIS + TPZ

Treatment plan were reviewed **QARC** Correlation of **Compliance to Quality to oncological outcomes**

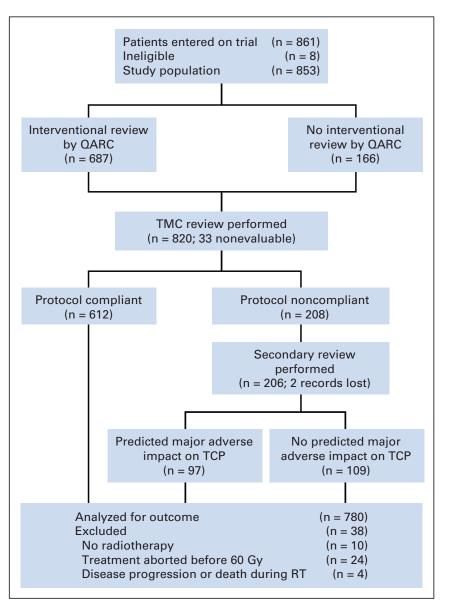
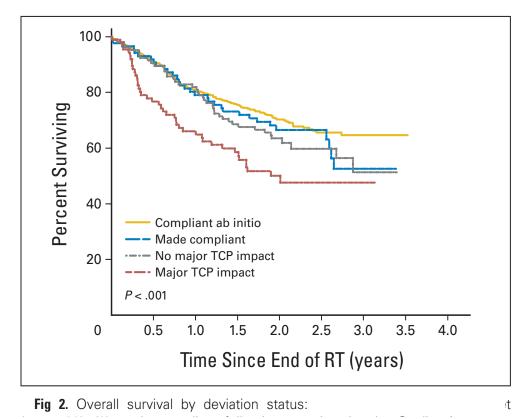


Fig 1. CONSORT flow chart showing sequence of reviews and analyses. QARC, Quality Assurance Review Center; TMC, Trial Management Committee; TCP, tumor control probability; RT, radiotherapy.

1. Radiotherapy Quality

RT quality compliance





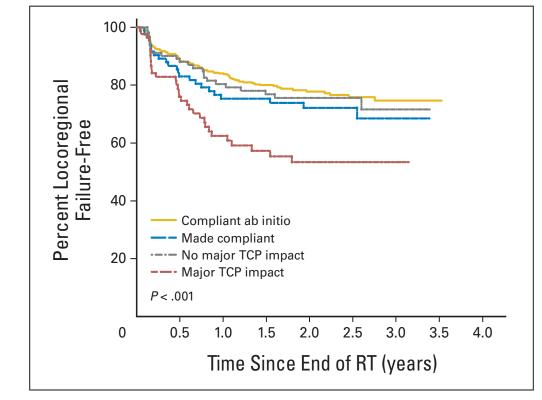


Fig 3. Time to locoregional failure by deviation status. T

- 24% in 2y LRFF

Peters et al. J Clin Oncol 2010

breast CANCER

2. Comorbidities

40 BC patients SIB-IMRT (50 Gy WB, 60 Gy TB) Age ≥ 70 years, pT1-2 pN0-1, M0, no neo-CT **Charlson comorbidity index**.

Fiorentino A et al. Aging Clin Exp Res 2018

 Table 2 Correlation with RT acute side effect (G2 skin toxicity)

Parameters	No. of cases	р
Age < 75	4	p = NS
Age > = 75	6	
CCI 0	1	p = 0.01
CCI≥1	9	
Breast volume <700 cc	2	p = 0.04
>700 cc	8	
Chemotherapy	4	p = NS
No chemotherapy	6	

CCI Charlton comorbidity index, NS no significant

Comorbidities:

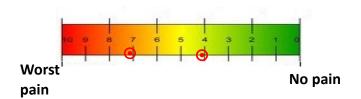
CCI 1 9 pts (22.5%), two patients a CCI 2 2 pts (5%), a CCI 3 2 pts (5%)

Most common comorbidities:

diabetes, ulcer disease, chronic pulmonary disease, and connective tissue disease.

2. Medications

- 74 years old
- ECOG 2
- BONE METASTASIS (prostate cancer)
- Moderate Pain (NRS max 7/10) at sacral level

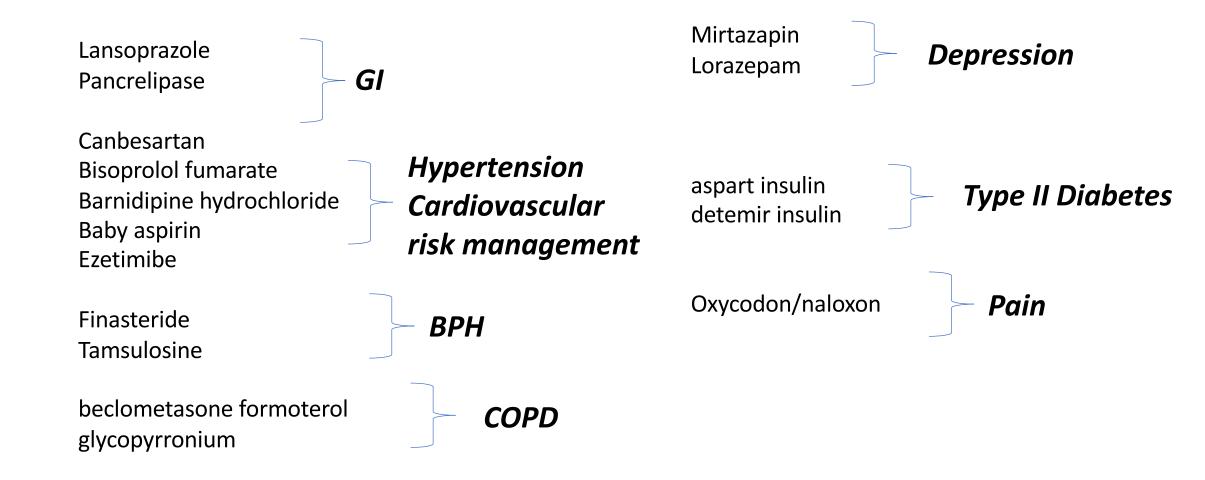


Multimorbidity:

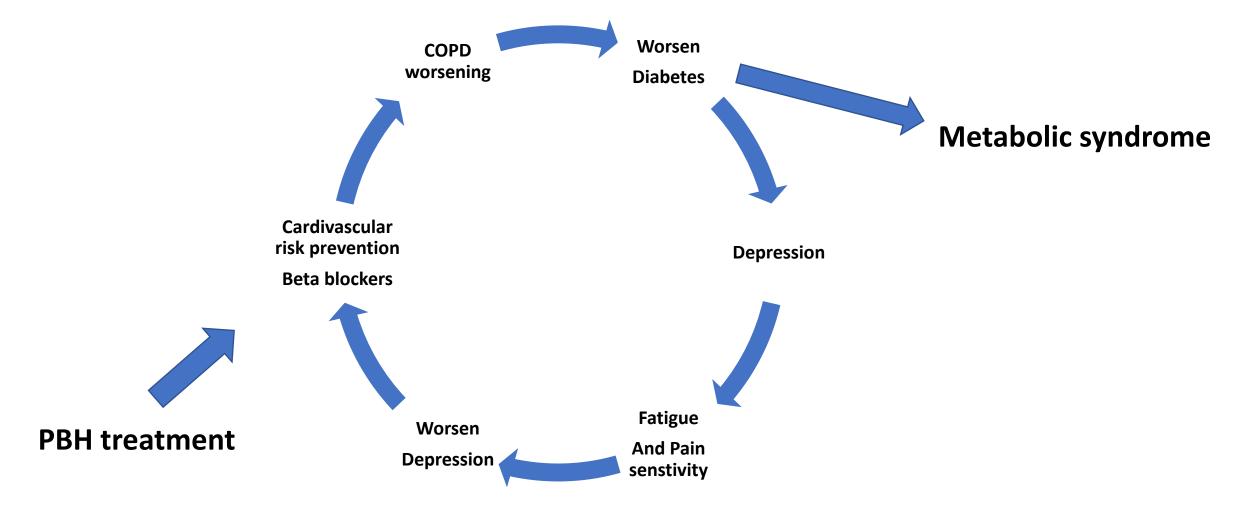
Metabolic syndrome /Diabetes -Type II/ COPD/ Hiatal hernia/BPH /Depression

2. Medications

Polipharmacy



2. Medications



Onco-geriatric evaluation of the patient

cervix CANCER

3. Socio-economics Factors

120 patients with cervical cancer Definitive CRT Questionnaires

Table 1
Socio-demographic characteristics of patients

Socio-demographic characteristics of patients	Total (<i>n</i> =120)	Compliant patients $(n=84)$	Non-compliant patients $(n=36)$	<i>P</i> - value
Mean age (SD) 5 Education level	1 (11.9)	52 (12.3)	48 (10.4)	0.078
Never gone to school	8	6 (75%)	2 (25%)	0.885
Up to primary school (incomplete/complete)	83	57 (69%)	26 (31%)	
Secondary/Tertiary (incomplete/complete) Marital status	29	21 (72%)	8 (28%)	
Married	65	45 (69%)	20 (31%)	0.970
Single	11	8 (73%)	3 (27%)	
Widow/Divorced	44	31 (71%)	13 (29%)	
Household size				
1–2	34	27 (79%)	7 (21%)	0.008
3-5	63	47 (75%)	16 (25%)	
6-12	23	10 (44%)	13 (57%)	
Position within household	d			
Head	42	27 (64%)	15 (36%)	0.490
Wife	63	45 (71%)	18 (29%)	
Other	15	12 (80%)	3 (20%)	
Poverty status				
Non-poor	66	52 (79%)	14 (21%)	
Poor	54	32 (59%)	22 (41%)	0.020
Type of dwelling				
Adequate	85	65 (77%)	20 (24%)	0.016
Inadequate	35	19 (54%)	16 (46%)	
Type of occupation of pa	tient			
Employed without social protection	45	29 (64%)	16 (36%)	0.532
Unemployed	16	11 (69%)	5 (31%)	
Inactive	59	44 (75%)	15 (25%)	
Health coverage				
No	91	61 (67%)	30 (33%)	0.209
Yes	29	23 (79%)	6 (21%)	
Stage ^a				
I	11	9 (82%)	2 (18%)	0.538
II	68	45 (66%)	23 (34%)	
III–IV	39	28 (72%)	11 (28%)	

Arrossi S et al. Gynecologic Oncology 2007

^a Missing data for 2 cases.

Household size

Poverty status

Type of dwelling

cervix CANCER

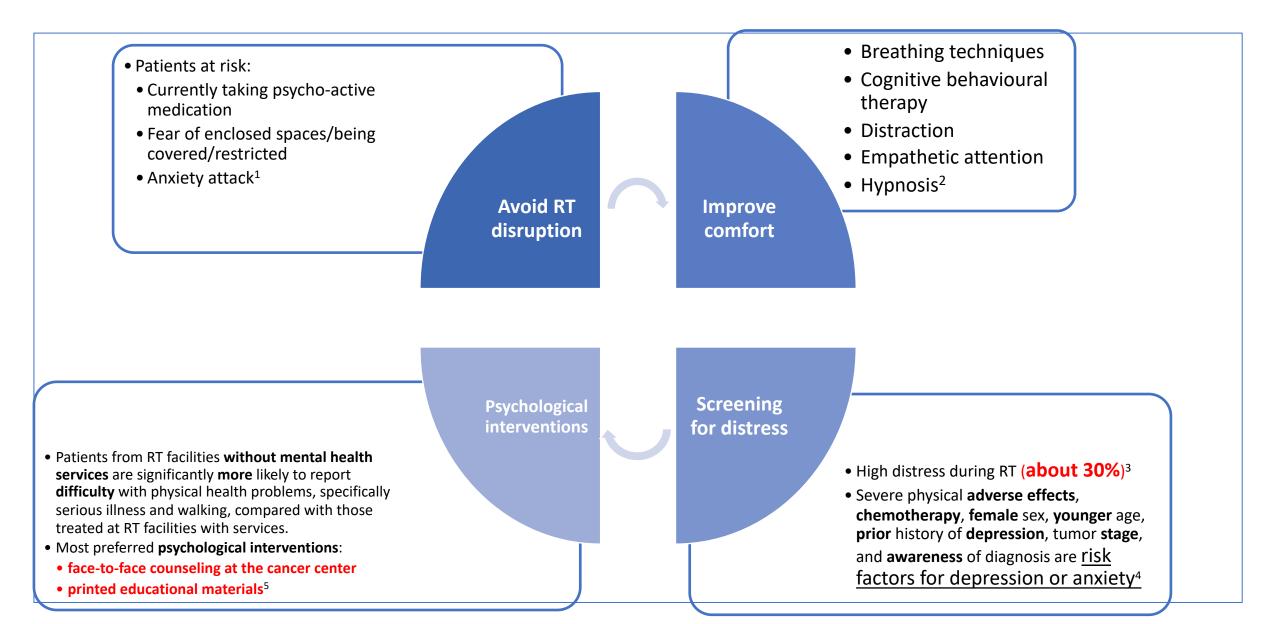
3. Socio-economics Factors

Table 3

Univariate and multivariate associations between socio-economic impacts and non-compliance

. Socio-economics factors		Impact on	Univa	riate analysis		Multiv	variate analys	sis
		patient's household	OR	95% CI	<i>P</i> -value	OR	95% CI	P-value
	Work interruption	Work interru	ption					
	work interruption	No	1.0					
		Yes	3.5	1.5 - 8.2	0.003			
	l	Reduction ir		vorked				
		No	1.0	0 2 1 2	0.202			
		Yes Storting poid	0.6	0.3–1.3				
120 patients with cervical cance	r	Starting paid No	1.0		0.282			
120 patients with cervical cance	•	Yes	1.8	0.6-5.1	0.202			
Definitive CRT		Increase in h						
		No	1.0		0.556			
Questionnaires		Yes	0.7	0.2 - 2.6				
Questionnalles	Loss of family income	Loss of fami	•	ie				
	,	No	1.0		0.000	1.0		0.000
		Yes	3.1	1.4-7.0	0.006	3.8	1.5-9.5	0.003
	•	Problems in No	1.0	or education	0.367			
		Yes	1.5	0.6-3.7	0.507			
		Absences fro						
	Absence from school	No	1.0			1.0		
		Yes	4.3	1.8-9.9	0.001	3.6	1.4-9.1	0.005
			a daily co	onsumption o				
		No	1.0		0.158			
		Yes	1.8	0.8-3.9				
		Delays in pa No	iyments 1.0		0.079			
		Yes	2.0	0.9-4.5	0.079			
		Sale of prop						
		No	1.0	or suvings	0.743			
		Yes	0.9	0.4-1.9				
		Change of c	hild care	organization				
		No	1.0		0.203			
Arrossi S et al. Gynecologic Oncology 2007		Yes	2.0	0.7–5.9				

4. PERSONAL sphere: PSYCHOLOGICAL STAPLES FOR AN OPTIMAL RT DELIVERY



Definition and background

Conditioning Factors

New Technologies

Intervention strategies

RT improvements in the past 30 years

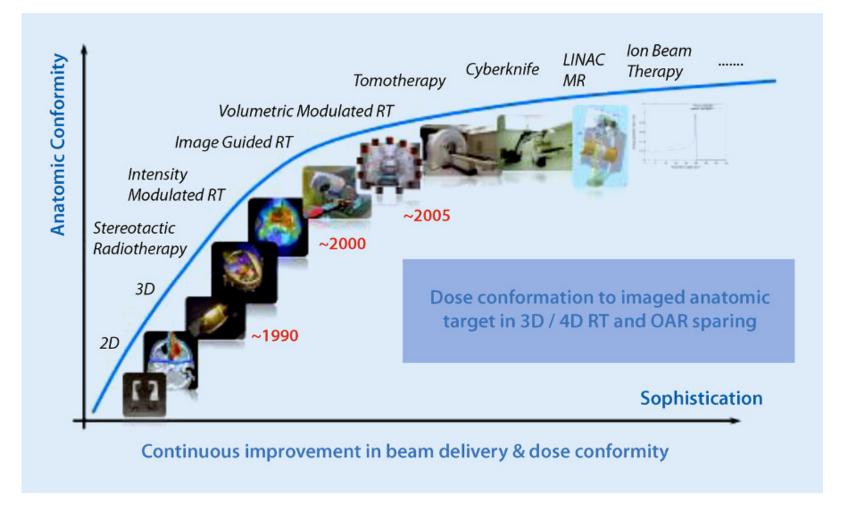
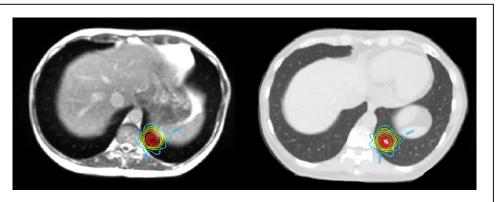
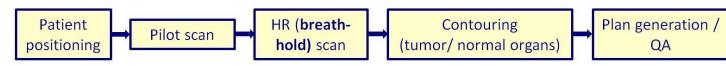


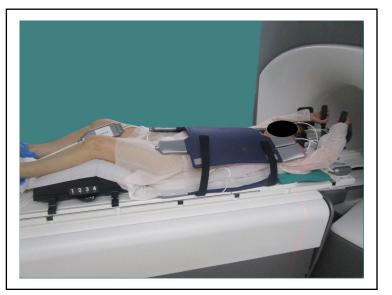
Fig. 1 ▲ Improvement in radiotherapy (*RT*) during the past three decades. *MR* magnetic resonance, *OAR* organ at risk Herrmann H et al. Radiologe 2019

MRgRT work-flow

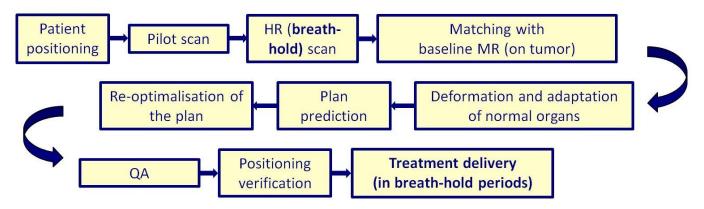


Simulation:





For each fraction:



Tetar et al. Cureus 2018

MRgRT TIME for treatment delivery

	Overall $(n = 30)$	Palliative $(n = 4)$	No CGA $(n = 13)$	CGA (n = 13)	þ Value or χ² test (CGA vs no CGA)	SBRT	IMRT	þ Value (SBRT vs IMRT)
Age, y	81.4 ± 3.4	81.0 ± 3.7	81.7 ± 3.7	81.2 ± 3.3	0.73	81.6 ± 3.4	80.9 ± 3.7	0.6
Women	10 (33.3)	2 (50.0)	5 (38.5)	3 (23.1)		4 (33.3	6 (35.3)	
Wheelchair	3 (10.0)	0 (0.0)	2 (15.4)	l (7.7)		2 (16.7)	l (6)	—
Cognitive	2 (6.7)	0 (0.0)	0 (0.0)	2 (15.4)		4 (33.3)		—
impairment						_		
Number of	of		± 9.3	7.5	± 2.9	l (8.3)	l (6)	—
						5.4 ± 1.4	3.9 ± 2.7	<0.001
fractions						72		0.000
		- 0(– 7 0			7.3 ± 2.8	12.5 ± 6.0	0.002
Beam on 1	time," mi	n 9.6	• ± 7.0	14.0	± 9.3	0.4 ± 0.1	0.3 ± 0.1	0.06
Beam on t	timo ^a /	35 0) ± 12.6	430	± 13.0			
			- 12.0	чЭ.0	- 15.0	: body radiatio	on therapy.	
effective t	ime. ^b mir	า					.,	
	,	-				approach.		

Table 2.	Baseline	characteristics	of the sample.	
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[•]Effective time: treatment duration considering also the time during which target volume is out of the delivery position using a gating approach.

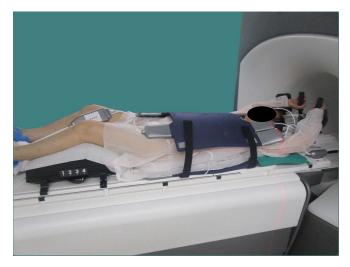
Boldrini L. et al. Rad Med 2020

MRgRT PATIENTS complaints

	Yes	Considerable
Noise	60% (N = 90)	17% (N=26)
Cold	29% (N = 44)	10% (N = 15)
Paresthesia	28% (N = 42)	6% (N = 9)
Dizziness	11% (N = 16)	1 % (N = 2)
Local heat sensations	9% (N = 13)	1 % (N = 2)
Metallic taste	2% (N = 3)	-
Light flashes	2% (N = 3)	-

Tetar S. et al Cureus 2018

MRgRT patients SELECTION



Patients should be divided in:

- **physically not compatible** (i.e. pace maker carriers);
- clinically not compatible (i.e. major psychiatric disorder, severe claustrophobia);
- **border line compatible** (i.e. mild claustrophobia);
- fully compatible

Appropriate intervention should be considered in **border line compatible** patients (e.g. psychological intervention or patients support techniques such as music or aromatherapy).

Patients evaluated as **not compatible** or **refusing** hybrid treatment should be directly addressed to **standard RT delivery units**.

MRgRT Patient SELECTION

MASTER score

MRI-Guided Radiotherapy Selection Elderly

Dedicated MR compatibility scoring systems are useful to avoid *a priori* choice based on clinical or age related variables
 Table 3. MASTER score items and corresponding values.

Condition	MASTER score value
MRI incompatibility (i.e. pacemaker)	4
Major cognitive impairment	4
Severe claustrophobia	4
ECOG PS value ≥3	3
ECOG PS value ≥2	2
Mild cognitive impairment	L
Frailty	Í.
Essential tremor	L
Visual deficit	L
Deafness	I
Gated treatment foreseen	L
Urinary or fecal incontinence	L

ECOG PS: Eastern Cooperative Oncology Group Performance Status; MRI: magnetic resonance imaging.

Definition and background

Influencing Factors

New Technologies

Intervention strategies

DISTRACTIVE therapies

Distraction as a Complementary Therapy for Cancer

What is distraction?

Distraction draws a person into a highly interesting activity to take his or her mind off pain or discomfort.

Can distraction help people with cancer?

Distraction has been found to help when people are experiencing anxiety, nausea, or pain. It does not cure cancer. But it has been shown that distracting a person's mind from unpleasant thoughts, procedures, or pain may help them feel better.

How does distraction work?

Many different types of activities and therapies can provide distraction. Some of them have other therapeutic benefits, too. These activities and therapies include:

How does distraction work?

Many different types of activities and therapies can provide distraction. Some of them have other therapeutic benefits, too. These activities and therapies include:

- Art therapy
- Music therapy
- Dance therapy
- Imagery
- Stories
- Relaxation therapy
- Virtual reality and computer games

Distractive therapies in children

Movie making as a cognitive distraction for paediatric patients receiving radiotherapy treatment: qualitative interview study

PEDIATRICS

Movie-Making Program (MMP)

children produce a short creative video describing each patient's journey in their own words

ARTICLE SUMMARY

Article focus

- Independent analysis of a programme where children with cancer make a movie about their radiation therapy experience.
- Qualitative description of semistructured interviews with parents of programme participants.

Key messages

- A range of benefits were attributed to making a movie including reductions in the child's anxiety and increased willingness to receive treatment.
- Further benefits were attributed to sharing the movie including maintaining social engagement and aiding school reintegration.
- The family and others in the child's social network also benefited.

Strengths and limitations of this study

- Independent analysis by a team experienced in healthcare evaluation.
- Open-ended questions yielded rich information.
- Only the perspectives of parents were analysed, not those of the children themselves.
- Only parents of children with favourable treatment outcomes were interviewed.

Shrimpton B et al. BMJ Open 2013

Distractive therapies in Interventional Radiotherapy

Original paper

HAPPY – Humanity Assurance Protocol in interventional radiotheraPY (brachytherapy) – an AIRO Interventional Radiotherapy Study Group project

Clinical Investigations

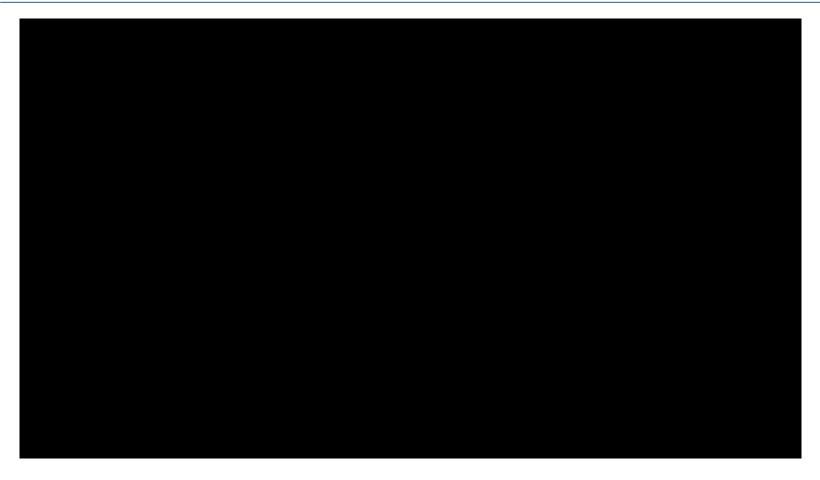
Valentina Lancellotta, MD¹, Vitaliana De Sanctis, MD², Patrizia Cornacchione, MSc¹, Fernando Barbera, MD³, Vincenzo Fusco, MD⁴, Cristiana Vidali, MD⁵, Sara Scalise, MSc¹, Giulia Panza, MD⁶, Angela Tenore, MSc¹, Giuseppe Ferdinando Colloca, MD¹, Renzo Corvò, MD⁷, Maria Antonietta Gambacorta, MD^{1,6}, Stefano Maria Magrini, MD⁸, Luca Tagliaferri, MD¹

	Patient's needs/issues general clusters	HAPPY interventions/recommendations
1	Lack of information and the fear of "unknown"	Procedure information booklet, possibly with FAQs, and sharing patient story, to be delivered many days before the therapy Improving the patient's participation in therapeutic choices also using decision support tools and discussing predictive models
2	Comfortable and relaxing environment	Possibility of hearing music chosen by the patient and/or watching relaxing videos
3	Ability to reduce anxiety	Psychological support in the interventional room and/or prescription of anxiolytics if necessary
4	Fear of the word "Bunker"	Use alternative words like "Interventional Room" or "Treatment Room"
5	Use of the word "Brachytherapy" often not known and heard for the first time by the patient	Use a more conventional term such as "interventional radiotherapy"
6	Embarrassment over external genital depilation (if necessary) in the interventional room	Suggestion to perform external genital depilation at home
7	Discomfort due to the long maintenance of the bladder catheter	The bladder catheter will be placed in the interventional room just before the procedure
8	Sense of loneliness in the room	If possible, an operator holds the patient's hand during the applicator positioning and plans optimization making human proximity perceived





Patient's compliance in Interventional Radiotherapy









MultISenSory Integrated system for patient cOmpliaNce improvement









Patient's compliance: the Art 4 ART project

Confortable and relaxing environment Sensorial experience during patient disease journey Patient Profiling Relating pt ART_PATH with exams/tox/interruption Proactive action proposals

MRO. ART

Innovative treatments and patients compliance 31° RESIDENTIAL COURSE

12 NOVEMBER 2021 virtual 22-23 NOVEMBER 2021 onsite and virtual 26 NOVEMBER 2021 virtual

Scientific Coordinators: Vincenzo Valentini Maria Antonietta Gambacorta, Luca Indovina Honorary Presidents: C.A. Perez, N. Cellini

Opening lecture (recorded) Moderators: A.G. Morganti, G. Macchia Omics sciences and compliance to radiotherapy: is there a link? C.N. Andreassen

Keynote lectures

Image guided radiotherapy technologies and treatment compliance Compliance between innovation and clinical experience: health economics perspective What is considered innovation in 20's radiotherapy? Compliance to treatments using stereotactic technologies FLASH therapy and compliance: a new era? Immunotherapy and radiotherapy: efficacy, innovative fractionations and compliance Particle therapy and patient compliance

TOPICS

Metrics: Which compliance to be measured? Metrics: Which compliance is important for the patient undergoing radiotherapy?

Actions: Will innovation change compliance in radiotherapy treatments? Actions: Big Data and AI: which contribution to compliance? Actions: Does drug innovation change compliance in combined treatments?

Focus on: Prostate cancer innovation and compliance Focus on: H&N cancer innovation and compliance Focus on: Combined radio-chemotherapy treatments in third stage lung cancer Focus on: Lung cancer innovation and compliance Focus on: Breast cancer innovation and compliance Focus on: Anal cancer innovation and compliance

Poltrona Turchese: Giglio – Gentilezza

Poltrona Blu:

Compliance SAVES

Poltrona Azzurra Oriensio - Amore

Obedience Conformity Accordance Cooperation Resilience

Poltrona Verde Chial Tulipono – Onesto

Resilience CURES

15 사람이 가지 않는 것이 같은 것이 같은 것이 같은 것이 같이 많이 많이 많이 했다.