FOCUS IN CARDIONCOLOGIA

L'oncologia oggi: breve introduzione per i cardiologi

Le esigenze dei radioterapisti

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Key point:

We need cooperation between radiation oncologist and cardiologist

Risk of cardiotoxicity after radiotherapy

Radiotherapy in patients with pacemakers and implantable cardioverters-defibrillators

Background: thanks to their longevity, patients treated with RT for breast cancer and Hodgkin's L are at risk of heart complications

Accelerated atherosclerosis
Inflammation
Fibrosis
Fibrosis/Damage of the AV node and conduction system

Myocardial infarctions
Pericarditis
Congestive heart disease
Valvular disease
Arrhythmias

The NEW ENGLAND JOURNAL of MEDICINE

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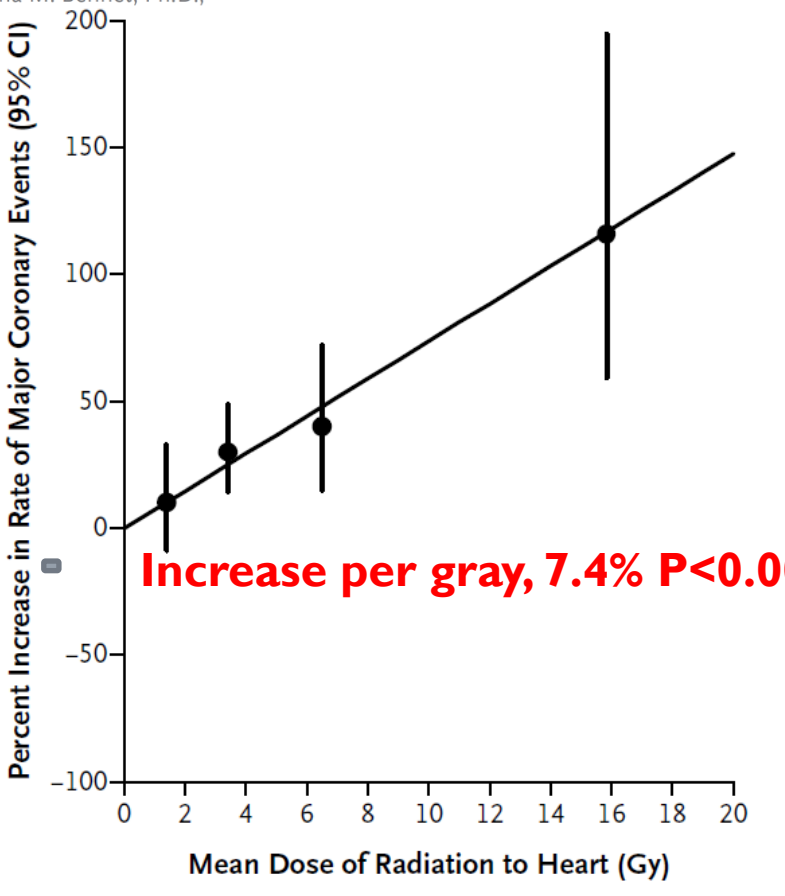
Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D.,

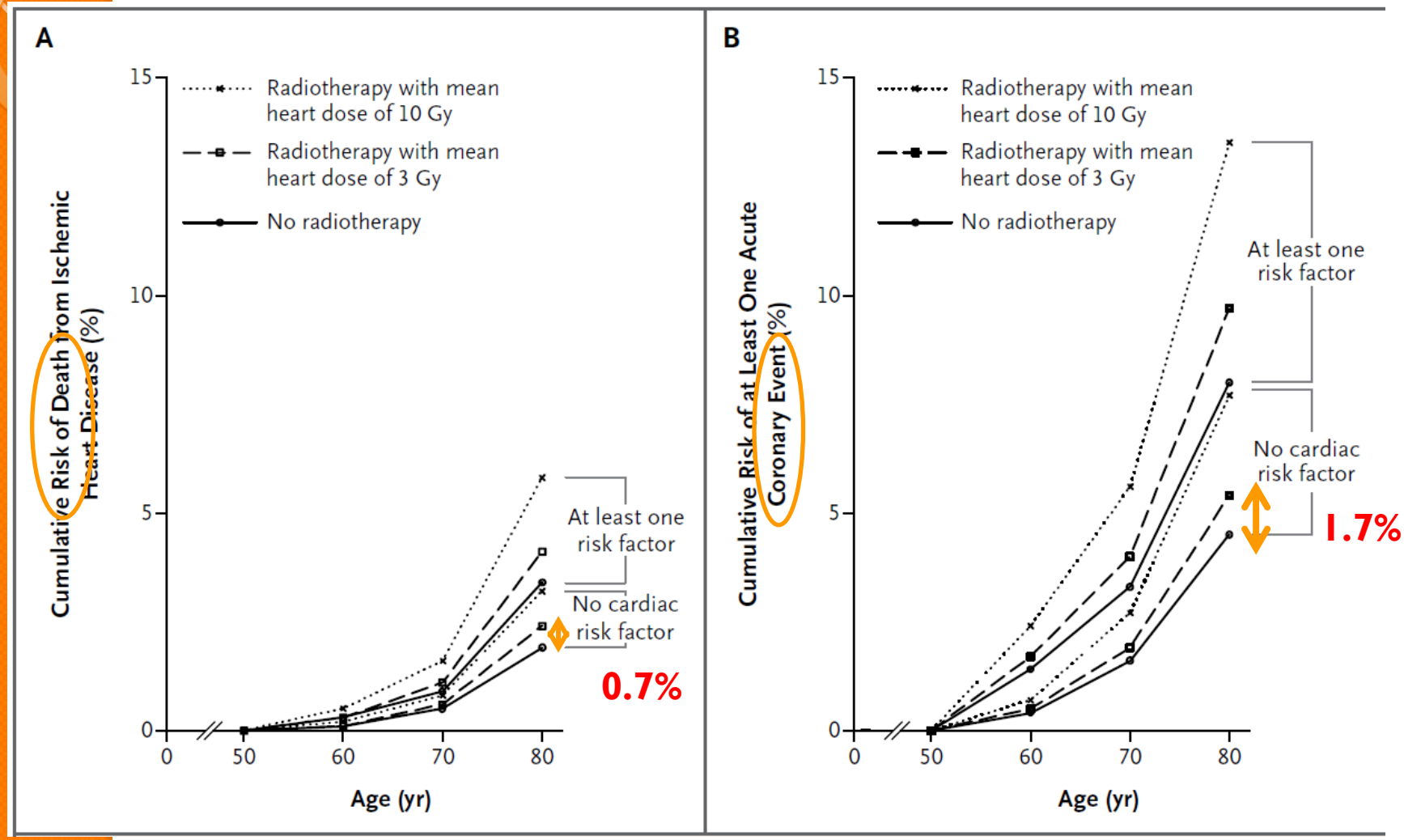
2168 women
From 1958 to 2001

Rate of Major Coronary Events According to Mean Radiation Dose to the Heart, as Compared with the Estimated Rate with No Radiation Exposure to the Heart



Darby, et al, NEJM 2013

Risk by age 80 of RT at age 50



International Journal of Radiation Oncology biology • physics

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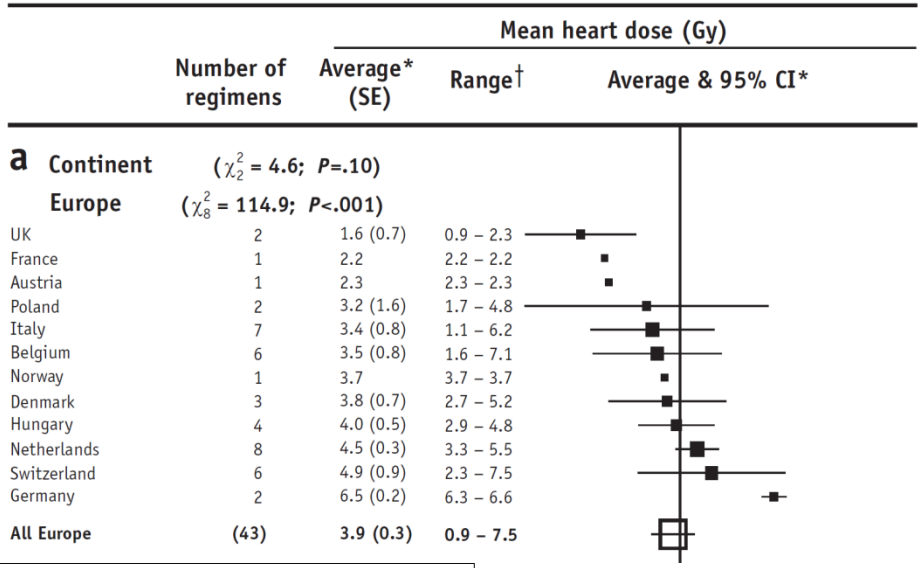
2015

Clinical Investigation

Exposure of the Heart in Breast Cancer Radiation Therapy: A Systematic Review of Heart Doses Published During 2003 to 2013

Carolyn W. Taylor, DPhil, FRCR,* Zhe Wang, PhD,*

Mean heart dose < 4Gy



	Number of regimens	Mean heart dose (Gy): Average* (SE)	Range†	Average & 95% CI*
a Continent	(χ^2_2 = 4.6; *P*=.10)			
Europe	(χ^2_8 = 114.9; *P*<.001)			
UK	2	1.6 (0.7)	0.9 – 2.3	
France	1	2.2	2.2 – 2.2	
Austria	1	2.3	2.3 – 2.3	
Poland	2	3.2 (1.6)	1.7 – 4.8	
Italy	7	3.4 (0.8)	1.1 – 6.2	
Belgium	6	3.5 (0.8)	1.6 – 7.1	
Norway	1	3.7	3.7 – 3.7	
Denmark	3	3.8 (0.7)	2.7 – 5.2	
Hungary	4	4.0 (0.5)	2.9 – 4.8	
Netherlands	8	4.5 (0.3)	3.3 – 5.5	
Switzerland	6	4.9 (0.9)	2.3 – 7.5	
Germany	2	6.5 (0.2)	6.3 – 6.6	
All Europe	(43)	**3.9 (0.3)**	**0.9 – 7.5**	

Whole-heart dose: the most commonly reported measure

1.1 → 8.5 Gy

Average mean heart dose

Variability affected by:

- **Tecnique**
- More extensive **targets**
- Unfavorable **anatomy**
- **Interobserver variation** contouring

Reduction in cardiac exposure: Which technique?

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

2014

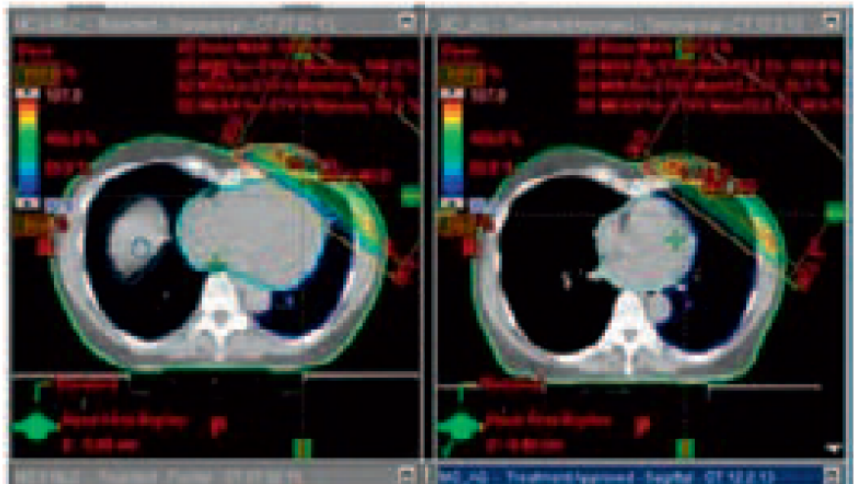
Review

Cardiac dose sparing and avoidance techniques in breast cancer radiotherapy

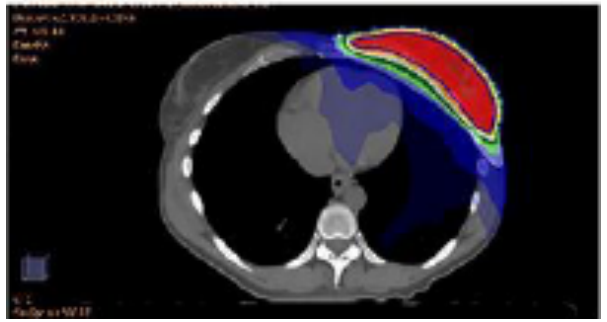
Chirag Shah [a], Shahed Badiyan [b], Sameer Berry [a], Atif J. Khan [c], Sharad Goyal [c], Kevin Schulte [a], Anish Nanavati [d], Melanie Lynch [a], Frank A. Vicini [e,*]

Prone breast radiotherapy

Deep-inspiratory **Breath-hold**

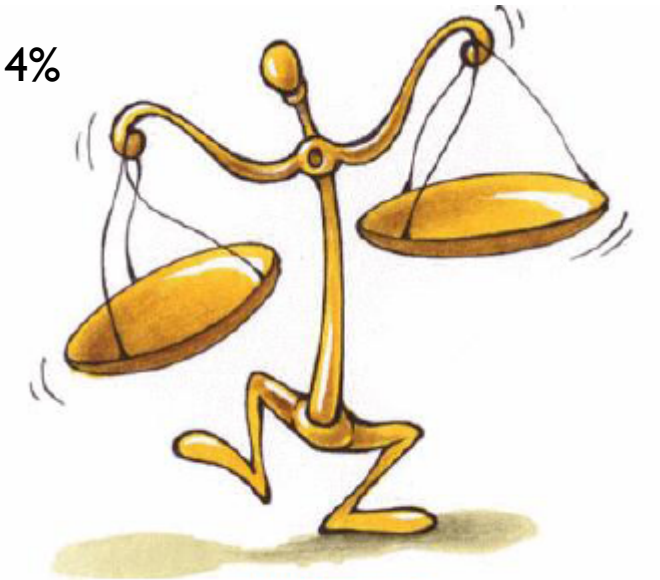


IMRT and **VMAT**



It is highly probable that the risk of radiation-related cardiac tox is lower than for patients treated in the past. The magnitude is uncertain

Benefits After BCS, RT reduces the absolute risk of breast cancer death at 15 years by 4%



Risks 50 years of age at RT, no cardiac risk factors mean heart dose of 4 Gy the absolute risk of radiation-related ischemic heart disease would be 0,6% for mortality

Cardiac risk can be estimated
Cardiac risk varies
For most women treated according to current guidelines, benefit outweighs cardiac risk.

Background:

There is a rising coincidence of patients aged
over 65 years undergoing radiotherapy for malignancies and implantation of cardiac pacemakers (PMs) and cardioverter-defibrillators (ICDs)

Radiotherapy is applied in up to 50 % of cancer cases

It can be assumed that the number of patients in need of both therapies is growing due to demographic changes.

Nitsche et al, Breast Care 2015

Hystorical american guidelines

Table 1 Guidelines of the American Association of Physicists in Medicine [5, 35]

Radiation source	a) No use of betatrons
	b) Due to lack of data for other sources, recommendations are given only for betatrons, linear accelerators, and telecobalt sources. Other radiation sources/qualities should only be used after individual risk assessment
Execution of radiation treatment	a) PMs should not be located directly in the beam
	b) The expected dose at the PM should be estimated before first treatment
	c) PM dose >2 Gy: PM interrogation before initiation of RT, once weekly. PM dose 2–10 Gy: early parameter changes might be indicative for imminent PM failure
Patient monitoring	a) Mandatory monitoring of the patient during first RT treatment

PM pacemaker, *RT* radiotherapy

RT changed from the use of primarily conventional techniques and conventional fractions to IMRT /ART and hypofractionation.

Modern CIEDs are still radiosensitive because of their increased circuit complexity

Marbach et al, Med Phys 1994

Potential errors in CIEDs

	Potential error	iac pacemaker	ICD
Ionizing radiation	Altered stimulation (amplitude, frequency		x
	Altered sensing (over-/under sensing		x
	Inhibition of stimulation (pause		x
	Change in operational mode		x
	Battery depletion (ERI-		x
	Altered electrode s	X	x
	Inhibition of a		x
	Altered (r		x
	Prolo		x
	I		x
		x	x
		x	x
		x	x
Electromagnetic in		x	x
	stole)	x	x
	ronous stimulation)	x	x
	ular pacing	x	x
	rrhythmia therapy		x
	therapy		x
	mming of device	x	x

Cardiac devices may be affected in two ways:
electromagnetic interference (EMI)
direct damage to the circuitry via ionising radiation,
both of which may cause temporary and permanent device malfunction
Changes within the device parameters as result of EMI are seen even
when the CIED is placed outside the RT treatment field

In vitro studies on cardiac implantable electronic devices

Author	Year	CIEDs	Type	Effects
Souliman [56]	1994	18 (15 × 1-chamber and 3 × 2-chamber system), various manufacturers	PM	Irreversible malfunction of all 2-chamber syste…etween 16.8 and 64.4 Gy; irreversible malfunction of eight …ystems between 25.2 and70 Gy
Wilm [66]	1994	20 (3 manufacturers)	PM	10 Gy: decrease of stimulatory am…of function; 90–300 Gy: 19× loss of functi…pability)
Röthig [50]	1995	3 manufacturers (no information reg. number of devices)	PM	Failure of all tested syste…
Mouton [43]	2002	96 (different models and manufacturers)	PM	Decrease in stim…30 Gy; intermittent l… and 90 Gy; irreversi… 170 Gy
Hurkmans [21]	2005	19 (4 manufacturers)	PM	Irrev…130 Gy (loss of stimula- t… significant sign of malfunc-
Hurkmans [20]	2005	11 (4 manufacturers)	IC…	…ween 1.5 and 120 Gy (shock delivery …oss of sensing); first significant sign of …k energy) at 0.5 Gy
Uiterwaal [62]	2006	11 (4 manufacturers)		…hen directly irradiated (starting from 0.5 Gy); …entricular fibrillation
Kapa [24]	2008	20 (3 manufa… CRT syst…		…ue to scatter radiation (4 Gy, 6 MV)
Hashii [14]	2012	10 IC…		…arranged around a water phantom; 2 ICDs in 140 cm distance: …ware failures in both locations, 8× more often with 18 MV compared with 10 MV; 14–20× more secondary neutrons with 18 MV compared with 10 MV; no difference in scatter radiation (18.8 mSv/10 MV vs. 20.23 mSv/18 MV)
Hashimoto [15]	2012	…	ICD	107 GyE proton radiation: only scatter radiation but still exposure to high rate of secondary neutrons; one ICD malfunction every 15 GyE (reset, reversible loss of function); no irreversible failures
Zaremba [67]	2014	10 PM …CD (explanted; 5 man…turers)	PM/ ICD	Increasing fractional doses up to 150 Gy; all CIEDS were placed in a phantom in the beam; 6/18 MV photons: 14 malfunction in 5 PM with 18 MV; one malfunction in PM with 6 MV (HR 9,11 [95 % (CI): 1.04–79.69]; no

In PMs, errors resulting in asystole > 10 s or even complete loss of stimulation were found at ≤ 1 Gy
Device failure was not predictable by a threshold dose

In vivo results with cardiac implantable electronic devices

Author	Year	*n*	Tumor entity or site	CIED	RT dose	Dose CIED/energy	Effects
Raitt [49]	1994	1	Thyroid cancer	PM	4.8 GyE neutrons	0.9 GyE	Uncontroll… frequency (runaw…
Tsekos [61]	2000	1	Neuroendocrine cancer right arm	PM	50.4/1.8 Gy	~50 Gy (PM in beam)/n.m.	…quency
Nibhanu-pudy [46]	2001	1	Breast cancer	PM	<60/2 Gy	1.8 Gy/6 MV	
Hoecht [17]	2002	3	Pelvic metastases	ICD	No information	<0…	…al-
Frantz [11]	2003	1	Breast cancer	PM	66/2 Gy		
John [22]	2004	1	Breast cancer	ICD			125 Ω
Thomas [59]	2004	1	Lung cancer				
Mitra [42]	2006	1	Lu…				…ction
Sepe [52]	2007	1					…ontrollable increa…
Nemec [45]	2007						(runaway ICD, 1… VT, necessi…
Mu…						…/V	No m…
						…ily …atter)/n.m.	
						…/ GyE …otons	0 GyE t… 69 …
					4/2 Gy		
				PM	30/3 Gy		
							…away
			Head and neck… thorax, ab… pelvi…				…=2, no ICD in
Zare… [68]	2010	1					…rming: "invalid data detected," no …ction detected
Ferrara [9]	2010						No malfunction
Wadasa-dawala [64]	2011	8	li… can…			…–60 Gy (PM partially in beam)/6–15 MV	No malfunction
Dasgupta [6]	2011	1	Cardi… ses (rig… and left …		…/2.5 Gy	0.26 Gy (leads in beam)/n.m.	Intermittent ventricular under sensing
Soejima [54]	2011	60	Head and … thorax, pelvis, breast cancer	PM	20–74 Gy	<2 Gy (*n*=59), >2 Gy (*n*=1)/15 MV	Reset into fallback mode (*n*=1), prostate cancer case

Placement of the CIED in the beam, energies > 6–10 MV, cause excessive formation of secondary neutrons that harm the RAM or CMOS particle radiation may be positive predictors of CIED failure

Radiotherapy has been shown to cause malfunction of CIEDs, ranging from inappropriate triggering, device reprogramming or device failure. Other investigators have reported a minimal effect of radiotherapy on CIEDs

Guidelines

Strahlenther Onkol (2015) 191:393–404
DOI 10.1007/s00066-015-0817-3

ORIGINAL ARTICLE

DEGRO/DGK guideline for radiotherapy in patients with cardiac implantable electronic devices

Benjamin Gauter-Fleckenstein · Carsten W. Israel · Marc Dorenkamp · Jürgen Dunst · Mattias Roser · Rainer Schimpf · Volker Steil · Jörg Schäfer · Ulrike Höller · Frederik Wenz

Clinical Oncology 26 (2014) 45–50

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

A National Audit of Current Cardiac Device Policies from Radiotherapy Centres across the UK

J.F. Lester *, L.M. Evans *, Z. Yousef †, A. Penney †, P.N. Brown ‡, R. Perks ‡

RADIATION ONCOLOGY

Hurkmans *et al. Radiation Oncology* 2012, **7**:198

REVIEW Open Access

Management of radiation oncology patients with a pacemaker or ICD: A new comprehensive practical guideline in The Netherlands

Coen W Hurkmans[1,8*], Joost L Knegjens[2,8], Bing S Oei[3,8], Ad JJ Maas[4,9,10], GJ Uiterwaal[5,9], Arnoud J van der Borden[6,10], Marleen MJ Ploegmakers[11] and Lieselot van Erven[7,12]

Risk assessment

- Delineation of the estimated radiation dose to a CIED implanted in typical left pectoral location depending

Risk groups:

RISK FOR CLINICALLY RILEVANT INTERACTION IN PM PATIENTS

	<2 Gy	2–10 Gy	>10 Gy
Non-pacemaker dependent	Low	Middle	High
Pacemaker dependent	Middle	High	High

RISK FOR CLINICALLY RILEVANT INTERACTION IN ICD PATIENTS

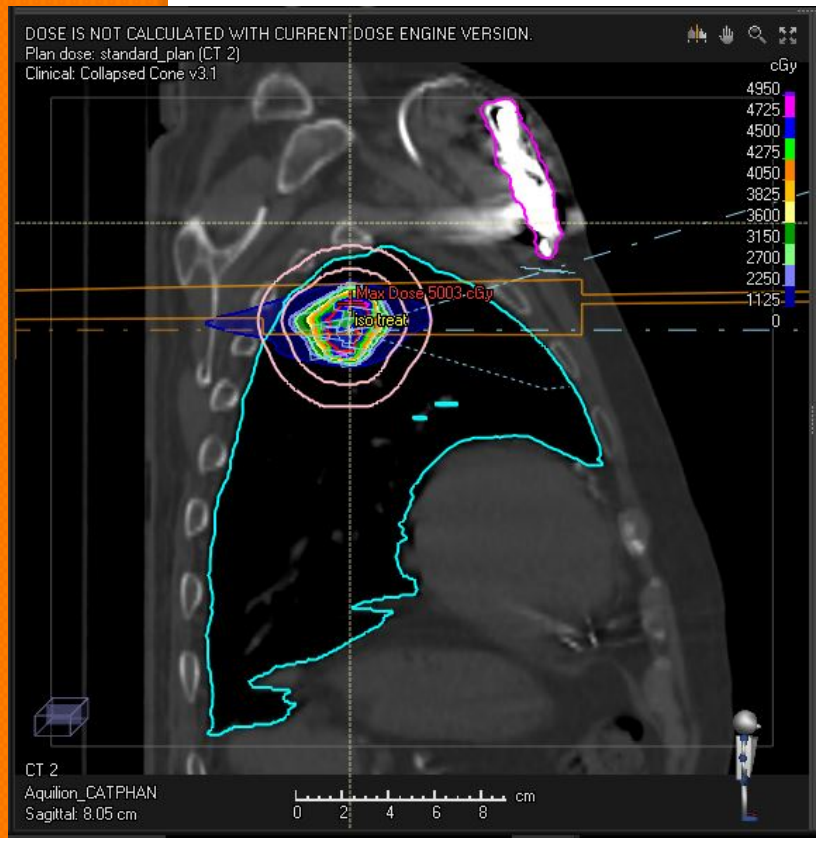
	<2 Gy	2–10 Gy	>10 Gy
ICD without VT/VFib	Low	Middle	High
ICD with VT/VFib before/after Implantation	Middle	High	High

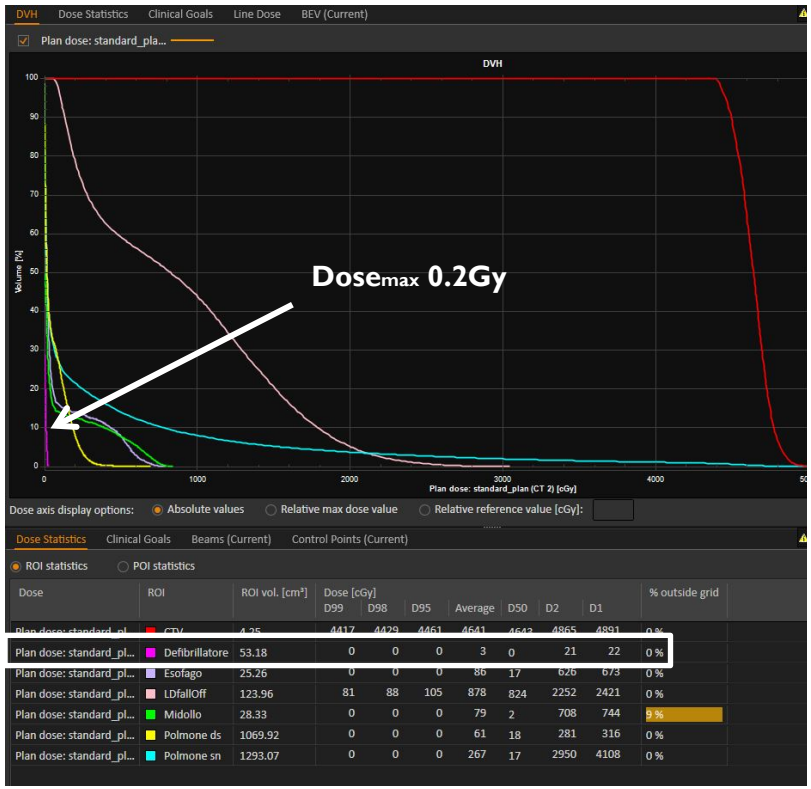
DEGRO guidelines, S&O 2015

CLINICAL CASES:

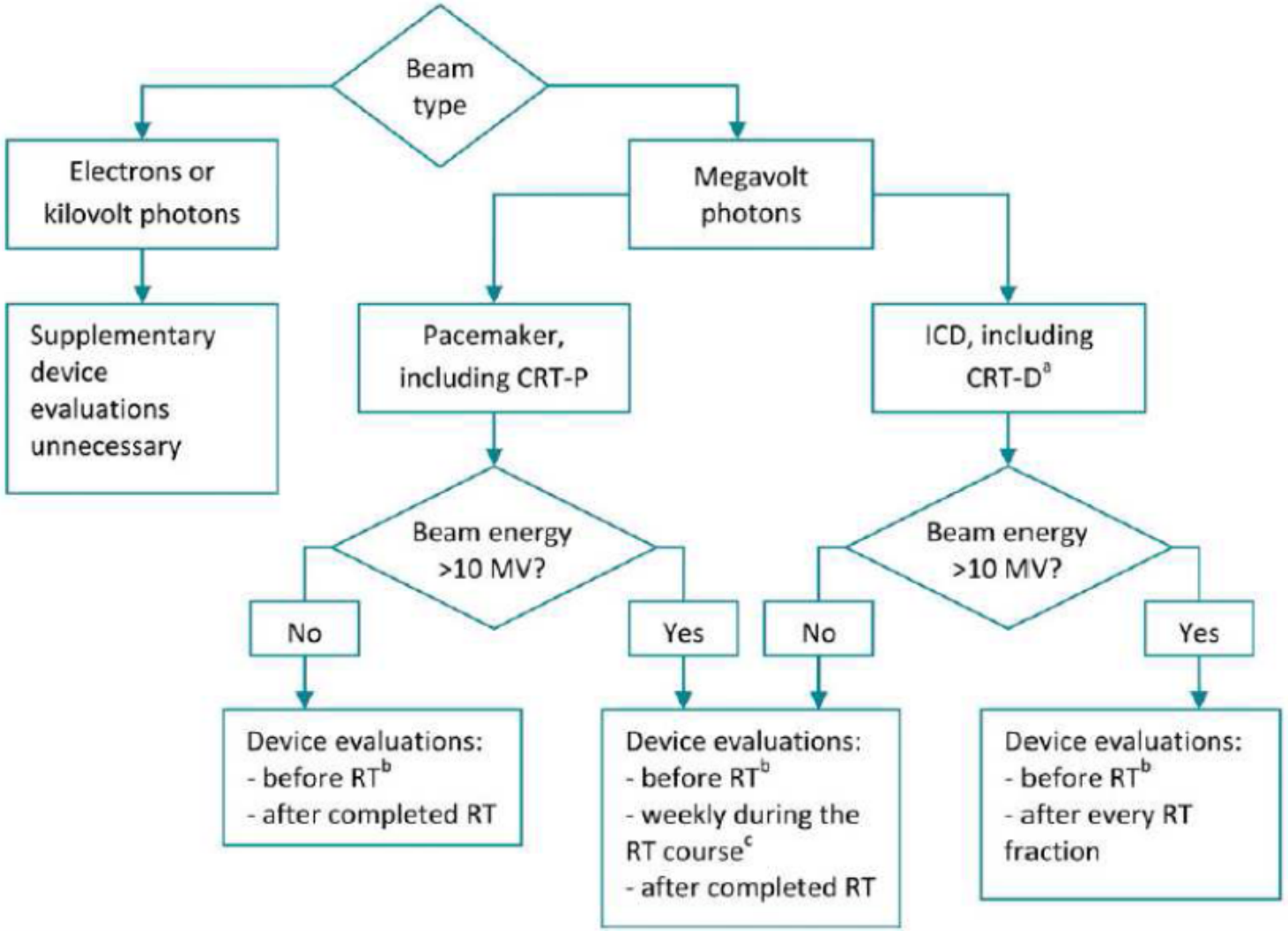
- Patient of 80 yrs
- Diagnosis of NSCLC of left lung, stage cT2N0M0
- Indication to stereotactic RT: 45 Gy, 15 Gy/fr.
- Heart stroke: ICD bicamerale Biotronix lumax 540

Magnet placement
Repetitive interrogation





Flowchart of suggested safety measures



Zaremba et al, Europace 2015

TEAMWORK

Measures before radiotherapy

- Identification of CIED in patient's chart, specification of CIED (manufacturer, model).
- The patient should be made aware of potential signs . In this case, patients should seek immediate advice with their treating cardiologist.
- Documentation of RT-associated risks in consent form.

- If CIED is located in beam: seek contact with treating cardiologist; discussion of relocation is advised
- Presentation at cardiologist: parameters, pacemaker-dependency.

- RT planning: acquisition of CIED in planning CT if feasible, limitation of energy to 6 MV (10 MV) when photons are used, computation/recording of cumulative radiation dose to CIED, no direct placement of CIED in beam.
- Classification into risk category (low, intermediate, high).

TEAMWORK

Measures during radiotherapy

- In vivo dosimetry at CIED during first fraction and comparison with calculated CIED dose.

- Pacemaker-dependent patients: consider asynchronous stimulation; either through reprogramming or magnet placement.
- ICDs: Deactivation of ATA therapy throughout each RT session; either through reprogramming or magnet placement
- Continuous audiovisual contact. Continuous ECG and SpO2 monitoring in patients with suspended ATA therapy and high-risk patients.
- Availability of cardiologist and programming device.
- Emergency protocol: immediate notification/activation of a reanimation team, high-risk patients need continuous presence of cardiologist, anesthesiologist, emergency physician.

- CIED interrogation after every RT session including reprogramming and reactivation of initial settings or antitachycardia therapy.

TEAMWORK

Measures after radiotherapy

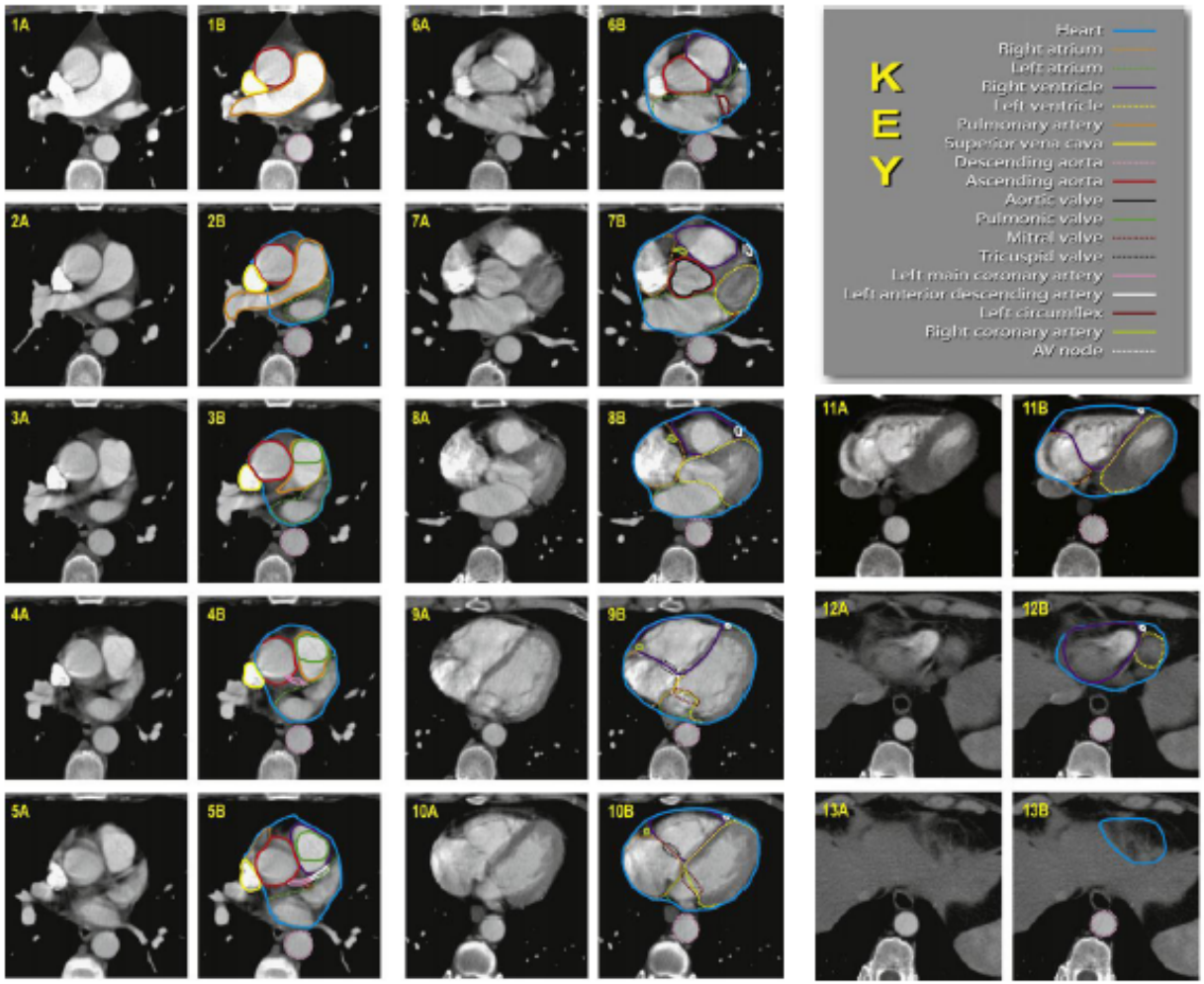
- Final interrogation (threshold levels, sensing and stimulation parameters, lead impedance, battery capacity), reprogramming of CIED.

- Analysis of any CIED irregularities in connection to RT and forwarding of data to manufacturer; even clinically nonsignificant changes in parameter settings may precede CIED defects.
- Exchange of CIEDs with significant defects even if the malfunction is temporary and full device recovery is observed.

- Repetitive interrogation 1, 3, and 6 months after RT; telemetric surveillance if available.

- Education of patient for clinical symptoms of CIED failure (irregular or slow cardiac rhythm, dizziness, syncope), emergency sounds emitted by CIED.

Grazie!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9B
5A
5B
10A
10B
KEY
Heart
Right atrium
Left atrium
Right ventricle
Left ventricle
Pulmonary artery
Superior vena cava
Descending aorta
Ascending aorta
Aortic valve
Pulmonic valve
Mitral valve
Tricuspid valve
Left main coronary artery
Left anterior descending artery
Left circumflex
Right coronary artery
AV node
11A
11B
12A
12B
13A
13B