

Recording Toxicity: the QUANTEC model

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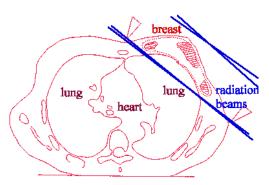


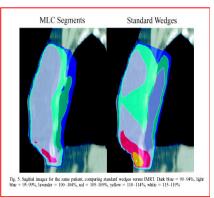


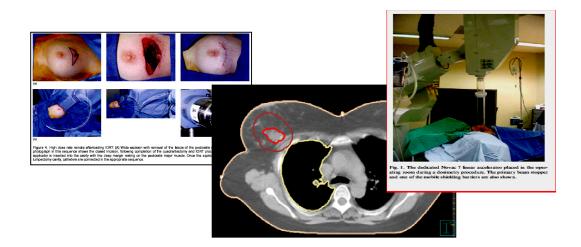


Breast cancer radiotherapy

- Many treated volumes
- Different treatment modalities
- Many treatment techniques
- Many fractionation schemes















An accurate toxicity evaluation is mandatory:

- To correlate and confirm (or not) the data derived from theoretical mathematical models (e.g., a/B ratio) with adequate clinical data
- To collect data to guide therapeutic decisions

 To compare the effectiveness and toxicities of the different treatment options



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• To *compare* the effectiveness and toxicities of the different treatment options



EDITORIAL

THE OMEGA ON ALPHA AND BETA

IJROBP 81 (2): 319-320, 2011

ELI GLATSTEIN, M.D.

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"OK, I confess: I have trouble with alpha/beta ratios, and I want to provoke some discussion.

The basic idea behind alpha/beta is a ratio of two different types of cell killing, essentially single hit and multiple hit types of radiation. This is what one gets with x-rays and the linear quadratic formula to explain a cell survival curve. That part is relatively understandable and straightforward.

The problem I have is when people propose to use alpha/betas for treatment of patients"

"Over the years, I have told many trainees that one can be an excellent clinical radiation oncologist and not necessarily know squat about alpha/beta. I believe that remains true today"

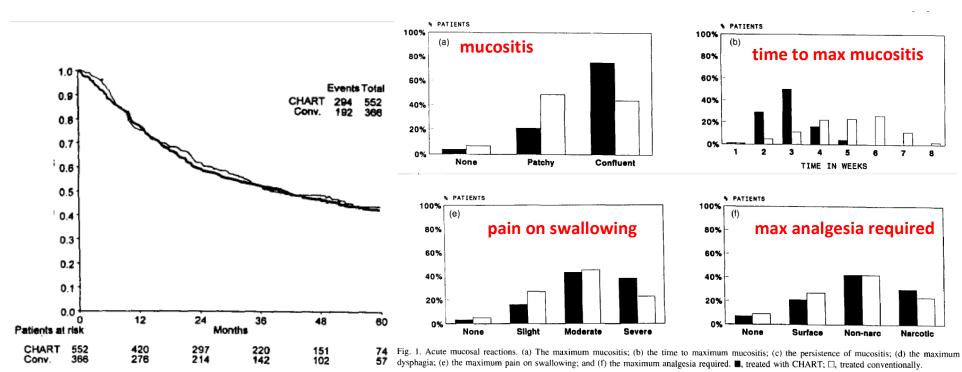






 The mathematical models for the prediction of response and toxicity were often clearly not confirmed by clinical data

CHART in head and neck cancer







Trial, 708 patients	recurrence (%)	fat necrosis(n.)
Wide field, 6 MV Whole breast, 15 ff / 40 Gy (2.6 Gy / fr)	11 %	2
Local field, e-, 10 MeV 6 x 8 cm, 8 ff / 42.5 Gy (5.3 Gy / frazione)	15 %	10



- "Care should be taken when applying models, especially when clinical dose/volume parameters are beyond the range of data used to generate the model/parameters.
- Models and dose/volume recommendations are only as good as the data available.
- Typically, they are based on dose-volume histograms (DVHs).
- DVHs are not ideal representations of the 3D doses as they discard all organ-specific spatial information"
- "RT-induced normal tissue responses are fraction size dependent "
- "....alfa/beta ratio is uncertain....."



- •.....When "Emami" was published, most external RT was delivered with opposing fields, and shrinking field techniques—the normal tissue was irradiated with a fairly uniform fraction size.
- •....use of sequential/concurrent chemotherapy/RT is increasing for many tumors.....
- •....Modern techniques often use multiple beams (with or without concurrent boosts);
- •....the volume of normal tissue exposed to low doses is often increased and the dose is delivered at fraction sizes ranging from 0 to the prescribed fraction size.
- •.....the duration follow-up is often inadequate to evaluate late toxicity



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the QUANTEC MODEL: IJROBP (76):3, 2010

Quantitative Analysis of Normal Tissue Effects in the Clinic

No skin No breast

Organ-Specific Papers

- 1. Brain
- 2. Optic Nerve/Chiasm
- 3. Brain Stem
- 4. Spinal Cord
- 5. Ear
- 6. Parotid
- 7. Larynx/Pharynx
- 8. Lung
- 9. Heart
- 10. Esophagus
- 11. Liver
- 12. Stomach/Small Bowel
- 13. Kidney
- 14. Bladder
- 15. Rectum
- 16. Penile Bulb

Vision Papers

True Dose Imaging Biomarkers Data Sharing Lessons of QUANTEC

- Clinical Significance- Describes the clinical situations where the organ is irradiated, and the incidence/significance of organ injury.
- Endpoints- Describes the different endpoints often considered when assessing injury, the impact of endpointselection on the reported injury rates, the challenges/utilities of different endpoints, and the time course of organ injury.
- Challenges Defining Volumes- Describes how the organ is typically defined (or segmented) on treatment planning images. Includes a discussion of uncertainties/challenges in organ definition (e.g. changes in organ volume/shape during therapy), and the associated impact on DVH's and dose/volume/outcome analyses.
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- Recommended Dose/Volume Limits- The available information is condensed into meaningful dose/volume limits, with associated risk rates, to apply clinically.
- Future Toxicity Studies- Describes areas in need of future study.
- Toxicity Scoring- Recommendations on how to score organ injury.





How?: the QUANTEC MODEL

Quantitative
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Organ-Specific Papers

Clinical aspects

- 3. Brain Stem
- 4. Spinal Cord
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OAR definition

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True Dose Imaging

Biomarkers

Data Sharing

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Data from literature

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Data about factors affecting the risk and about models used to predict the damage

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Recommendations about dose/volume

limits

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Future studies

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Toxicity scoring





RTOG acute toxicity

Tissue	G 1	G 2	G 3	G 4
Skin	Follicular, faint or dull erythema / epilation / dry desquamation / decreased sweating	Tender or bright erythema, patchy moist desquamation / moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis
Lung	Mild symptoms of dry cough or dyspnea on exertion	Persistent cough requiring narcotic, antitussive agents / dyspnea with minimal effort but not at rest	Severe cough unresponsive to narcotic antitussive agent or dyspnea at rest / clinical or radiological evidence of acute pneumonitis / intermittent oxygen or steroids may be	Severe respiratory insufficiency /
Heart	Asymptomatic but objective evidence of EKG changes or pericardial abnormalities without evidence of other heart disease	Symptomatic with EKG changes and radiological findings of congestive heart failure or pericardial disease / no specific treatment required	Congestive heart failure, angina pectoris, pericardial disease responding to therapy	Congestive heart failure, angina pectoris, pericardial disease, arrhythmias not responsive to nonsurgical measures





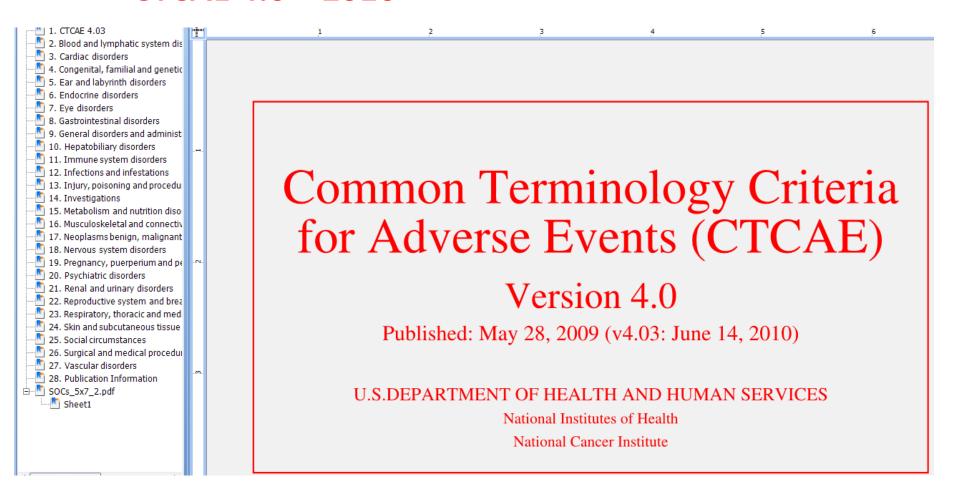
RTOG late toxicity

Tissue	G 1	G 2	G 3	G 4
Skin	Slight atrophy; pigmentation change; some hair loss	Patch atrophy; moderate telangiectasia; total hair loss	Marked atrophy; gross telangiectasia	Ulceration
Lung	Asymptomatic or mild symptoms (dry cough); slight radiographic appearances	Moderate symptomatic fibrosis or pneumonitis (severe cough); low grade fever; patchy radiographic appearances	Severe symptomatic fibrosis or pneumonitis; dense radiographic changes	Severe respiratory insufficiency / Continuous oxygen / assisted ventilation
Heart	Asymptomatic or mild symptoms; transient T wave inversion & ST changes; sinus tachy > 110 (at rest)	Moderate angina on effort; mild pericarditis; normal heart size; persistent abnormal T wave and ST changes; low ORS	•	1





CTCAE 4.0 2010







CTCAE 4.0 2010 – heart

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			Grade																
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Adverse Event Definition: A disorder ch	1 ir actorics	2	3	4	5				Skin an	d subcutaneo	us tissue disor	ders				
Respiratory, thoracic and mediastinal disorders - 0	d A	Ski	and subcutaneous t	issue disorders			1 1									
specify	d			Grade			1 1	_								
	Adverse Ext		2	3	4	6					Skin and subcu	ıtaneous t	tissue disorde	rs		
	Lipohypertrophy	Asymptomatic and covering <10% BSA	Covering 10 - 30% BSA and associated tenderness;	Covering >30% BSA and associated tenderness and	-	1			Advesa Evert				Orade			
			limiting instrumental ADL	narcotics or NSAIDs				Datas	Adverse Event in plantar	Minimal skin changes	or Ship shapana	(e.g., pooling.	Sovere skin chang		4	
	- 11		1	indicated; lipohypertrapity; limiting self-care ADL					a-pranaz odpacathosia synchomo	dermatitis (e.g., eryth	oma, blistors, blood	ing, edema, or	peeling, blisters, bl	ooding.		- 1
	Definition: A disorder	characterized by hypertrophy of the su	boutaneous adipose tissue at the	site of multiple subcutaneous inje	ations of insulin.					edema, or hyperkeral without pain	osis) hyperkeratosi Emiting instru		edema, or hyperke with pain; limiting s			- 1
	Nail discoloration	Asymptomatic; dinical or diagnostic observations on		-		·							ADL	- 1		- 1
	- 11	intervention not indicated			l	1		_	tion: A disorder character				· -		f the feet.	_
	Definition: A disorde	r characterized by a change in the color	of the nail plate.					Penor	trital ederna	Selt or non-pitting	Indurated or p	itting edems; otion indicated	Edema associated disherance: increa	with visual -		
	Skin a	and subcutaneous tiss	ue disorders													
			Grade		_											
dverse Event	1 ized by less of skin pigment.	2	3	4						Skin and s	ubcutaneous t		sorders			
ration	Mild incluration, able to move	Moderate indusation, able to 8	evere induration, unable to	Generalized; associated with	Death		Adverse Ex	on the same			-	Grade				
Panel.	skin parallel to plane (sliding)	alide akin, unable to pinch	ide or pinch skin; limiting	signs or symptoms of		Telangie		rent	Tolangioctasias cov	rodan Tolonoi	adasias covering	 	3		4	. 6
	and perpendicular to skin (pinching up)	skin: limiting instrumental ADL	int movement or orifice (e.g., outh, anus); limiting self	impaired breathing or feeding	1	Totalgo	POMB-M		<10% BSA		SA; associated with	I.		ľ		ľ
	(percent) up;		ene ADL						1		social impact	1		l		1
A disorder character	ized by an area of hardness in t	ha skin.				_			orized by local dilatatio	on of small vessels n	stufting in red discolor	ation of the ski	án or mucous memb	_		_
ration	Combined area of ulcors <1		ombined area of ulcors >2	Any size ulcar with extensive		Toxic op	sidiermal no	crolysis	1-	- 1		1			hing covering A with associated	Death
	on; nonblanchable erythema of intact skin with associated		r; full-thickness skin loss volving damage to or	destruction, tissue necrosis, o damage to muscle, bone, or					1	- 1		1			(e.g., erytherns,	1
	warmth or odoma		crosis of suboutaneous	supporting structures with or					1	- 1		1		purpura, or detachmen	epidernal	1
				without full thickness skin loss		Detrito	ar & element	ur observat	erized by greater than:	SINK total books akin	sons necessition of description	mir The most	forme in thought to			Tartion II
e: A clanaties character	I land by circumsteribed inflators	tory and necrotic erosive lesion on	tascia the ekin		' 1 III		the mucou			and the conjugation	area separación o ce	ina. The ayrio	active is mosgittion	oc a rigperse	crossing complex at	accord to
Johnson syndrome				Skin sloughing covering 10 -	Death	Urticaria	1		Urticarial lesions co		al lesions covering 10		sions covering	-		-
our sur syrumon				30% BSA with associated					<10% BSA; topical intervention indicate		A; oral intervention	>30% BSA; indicated	; IV intervention	l		1
				signs (e.g., erythems, purpurs, epidermal		Detrito	a: A element	ar charact	erized by an italy skin.	•			I seed and restricted	l unite		•
				detachment and mucous			d gulacutary				te: minimal, local or		nedically significant	Life-fiveats	ening	Death
	l	d	stachment)	membrane detachment)			s - Other, s		symptoms; ofinical o	or nonimus	sive intervention	but not imm	rediately life-	consequen	ces; urgent	
 A disorder character muccus membranes. 	ized by less than 10% total body	skin area separation of dermis. Th	e syndrome is thought to be a	hypersensitivity complex after	cting the skin				dagnostic observat intervention not indi		d; limiting age- tate instrumental ADL		; hospitalization or n of existing	intervention	n indicated	1
PECCUS INSPECTATION.									100000000000000000000000000000000000000	cano approp	Tage Title Control of Control		ion indicated:	l		1
									1	- 1		disabling; if ACK	limiting soft care	l		1
												Print.				_
	Popura	compined area of resions covering <10% BSA	covering 10 - 30% B&A:	combined area of resons covering >30% BSA;	I	T		adver	se events, frequently after	cting the upper trunk,	preading centripetally ar	rd associated wi	ith pruntus.			
Definition: A disorder ch	aracterize	covering < 10% DOA	blooding with traums	sportaneous bleeding				Scalp	pain	Midpain	Moderate pain		Severe pain; limitin	g self care	-	\neg
Hirsutism		characterized by hemorrhagic areas o	the skin and mucous membrane.	Newer lesions appear reddish in	color. Older lexions are usual	y a darker				l	instrumental /		ACI.	I		- 1
	a Rash acnelform	mually become a brownish-yellow color Papules and/or pustules	Papules and/or pustules	Papules and/or pustules	Papules and/or pustules	Death	1	_	tion: A disorder character throphy	Covering =10% BSA	Covering 10 -		Covering >30% BS	-		
	ps by	covering <10% BSA, which	covering 10 - 30% BSA, which	oovering >30% BSA, which	covering any % BSA, which			1		associated with	associated wi	th strine or	associated with plo			
	ы	may or may not be associated with symptoms of prunitus of		I may or may not be associated with symptoms of pruritus or	may or may not be associate with symptoms of pruritus or					telangioctasias or chu skin color	nges in advecal struct	ture loss		- 1		
		tendemess	tendemess; associated with	tenderness: limiting self sare	tenderness and are			Defini	tion: A disorder character		on and thinning of the ep	idennis and den	rnis.			'
			psychosocial impact; limiting instrumental ADL	ADL; associated with local superintection with oral	associated with extensive superintection with IV			Skin t	hyperpigmentation	Hyperpigmentation o		tation covering	-	-		\Box
				antibiotics indicated	antibiotics indicated; life-					<10% BSA: no psych impact	osocial >10% BSA; as psychosocial			- 1		
	Definition Astronto	coharacterized by an expedienced accordi	e and restricts torically accounts	in the acain proper sheet and	fireatoning consequences	1		Defini	tion: A disorder character				ion.	_ '		_ '
	DENISON: A OSCIDE	r characterized by an eruption of papule	s and pustures, typically appearing	an woo, sceep, upper crest and i	OWN.		, III	_	repopigmentation	Hypopigmentation or	Hypoplaments		1.			
									A11-1-10-10-10-10-10-10-10-10-10-10-10-10							
										depigmentation cove <10% BSA; no psych	ing depigmentation					





CTCAE 4.0 2010 – lung

	Respirate	ory, thoracic and me			
Adverse Event	,	2	Grade 3		5
dult respiratory distress	,		Present with radiologic	Life-threatening respiratory or	-
ndrome	T .	ľ	findings; intubation not	hemodynamic compromise;	Louisi
			indicated	Intubation or urgent	
				intervention indicated	1
etirition: A disorder charac auma or surgery.	terized by progressive and life-thro	ratening pulmonary distress in ti	he absence of an underlying pur	monary condition, usually follow	ing major
on anyery.		1		1	
	Respirat	ory, thoracic and m	ediastinal disorders		
			Grade	_	
Adverse Event	1	2	3	4	5
ronchial stricture	Asymptomatic; clinical or diagnostic observations only;	Symptomatic (e.g., rhonchi o wheezing) but without	Shortness of breath with strider; endoscopic	Life-threatening respiratory hemodynamic compromise;	
	intervention not indicated	respiratory distress; medical		intubation or urgent	
		intervention indicated (e.g.,	laser, stent placement)	intervention indicated	
		steroids, bronchodilators)	1	1	1
alatina: E danidal chara.	Sucress for a numerous not of the feet	Guar kilha			
	Respirate	ory, thoracic and me			
Adverse Event	1		Grade 3	1 4	
carseness	Mild or intermittent voice	Moderate or persistent voice	Severe voice changes		
Wall del Feloo	change; fully understandable;		including predominantly	ľ	1
	self-resolves	occasional reputition but	whispered speech	1	
	Respirato	ry, thoracic and me	diastinal disorders		
			Grade		
	1	2	3	4	5
Adverse Event					
	Asymptomatic; clinical or	Symptomatic (e.g., noisy	Limiting self-care ADL; stridor;	Life-threatening	Death
	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic (e.g., noisy airway breathing), but causing no respiratory distress;		Life-threatening consequences; urgent intervention indicated	Death
Adverse Event aryngoal stonosis	diagnostic observations only; intervention not indicated	airway breathing), but causing no respiratory distress; medical management	endoscopic intervention	consequences; urgent	Death
uyngoal stonosis	diagnostic observations only; intervention not indicated	airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids)	endoscopic intervention	consequences; urgent	Death
aryngoal stonosis efinition: A disorder charact	diagnostic observations only, intervention not indicated intervention and indicated testing of the larging	ainway breathingi, but causing no respiratory distress; medical management indicated (e.g., steroids) geal ainway.	endoscopio intervention indicated (e.g., atent, taser)	consequences; urgent intervention indicated	
aryngoal stonosis efinition: A disorder charact aryngopharyngoal	diagnostic observations only; intervention not indicated reized by a narrowing of the larying Mild symptoms; no anxiety;	ainway breathingi, but causing no respiratory distress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild	endoscopio intervention indicated (e.g., atent, taser) Severe symptoms; dysprea	consequences; urgent intervention indicated	Death
aryngoal stonosis efinition: A disorder charact	diagnostic observations only, intervention not indicated intervention and indicated by a narrowing of the larying	ainway breathingl, but causing no respiratory distress; medical management indicated (e.g., steroids) real sinway. Moderate symptoms; mild arroidty, but no dyapnas; abort duration of observation and or duration of observation and or	endoscopio intervention indicated (e.g., stent, laser) Severe symptoms; dyspnea and awallowing difficulty;	consequences; urgent intervention indicated	
aryngoal stonosis efinition: A disorder charact aryngopharyngoal	diagnosis observations only; intervention not indicated leazed by a narrowing of the larying Mild symptoms; no anxiety; intervention not indicated	ainway breathing), but causing no respiratory distress; medical management indicanded (e.g., steroids) geal ainway. Moderate symptoms; mild aroids), but no dyspreas; ahort duration of observation and or aroidy/se indicated; limiting	endoscopio intervention indicated (e.g., stent, laser) Severe symptoms; dyspnea and awallowing difficulty;	consequences; urgent intervention indicated	
ryngoal stenosis efinitos: A disorder charac aryngopharyngoal racethoala	diagnosis observations only; intervention not indicated anized by a narrowing of the laryn Mild symptoms; no anxiety; intervention not indicated	aimay breathing), but causing no respiratory dafress; medical management indicand (e.g., steroids) geal aimay; Moderate symptoms; mild ansiety, but no dyspress; ahort duration of observation and or ansiety/s indicated; limiting instrumental ADL.	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms: dyspnea and awallowing difficulty: limiting sett care ADL	consequences; urgent intervention indicated	
aryngoal stenosis efinition: A disorder charact aryngopharyngoal racethosia efinition: A disorder charact	diagnosis observations only; intervention not indicated leazed by a narrowing of the larying Mild symptoms; no anxiety; intervention not indicated	airway breathing), but causing no respiratory dafress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspneas; ahort duration of observation and or anxiety indicated; imiting instrumental ADI. tent sonsation in the area of the	endoscopic intervention indicated (e.g., shart, laser) Sovere symptoms; dyspina and swallowing difficulty; limiting self care ADL. laryngopharynx.	consequences; urgent intervention indicated Lite-threatening consequences	Death
ryngoal stenosis efinitos: A disorder charac aryngopharyngoal racethoala	diagnosis observations only; intervention not indicated anized by a narrowing of the laryn Mild symptoms; no anxiety; intervention not indicated	airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspenas; short duration of observation and or anxiety's indicated; limiting instrumental ADL tert sensation in the area of the Transient opisiods;	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms; dyspnea and seallowing difficulty; limiting self care ADL laryngopharynx. Recurrent episodes;	consequences; urgent intervention indicated Lite-threatening consequences Persistent or severe episodes	Death
aryngoal stenosis efinition: A disorder charact aryngopharyngoal racethosia efinition: A disorder charact	diagnosis observations only; intervention not indicated anized by a narrowing of the laryn Mild symptoms; no anxiety; intervention not indicated	airway breathing), but causing no respiratory dafress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspneas; ahort duration of observation and or anxiety indicated; imiting instrumental ADI. tent sonsation in the area of the	endoscopic intervention indicated (e.g., shart, laser) Sovere symptoms; dyspina and swallowing difficulty; limiting self care ADL. laryngopharynx.	consequences; urgent intervention indicated Lite-threatening consequences	Death
ryngsal stanosis elinikos: A disorder characi ryngopharyngsal acathosia elinikos: A disorder characi	diagnosis observations only; intervention not indicated anized by a narrowing of the laryn Mild symptoms; no anxiety; intervention not indicated	airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspenas; short duration of observation and or anxiety's indicated; limiting instrumental ADL tert sensation in the area of the Transient opisiods;	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms; dyspnea and amallowing difficulty; limiting self care ADL laryngopharynx. Focument episodex; roninvasive intervention indicated (e.g., breathing technique, pressure point schenique, pressure point.	consequences; urgent intervention indicated Life-threatening consequences Persistent or severe episodes associated with synoope; urgent intervention indicated (e.g., fiberoptic laryngaceup).	Death
ryngsal stenosis efintion: A disorder charact ryngopharyngsal acathesia efintion: A disorder charact ryngospasen	diagnosis observations only; intervention not indicated lenged by a narrowing of the larying Mild symptoms; no anxiety; intervention not indicated collect by an uncomfortable persis -	airway breathing), but causing in respiratory dafricas; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspinas; ahort duration of observation and or anxiety's indicated; limiting instrumental ADL teré sensation in the area of the Transient episode; interversion not indicated	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms; dyspnea and awallowing difficulty; limiting self care ADL laryngopharynx. Recurrent opisodes; nonincasive intervention indicated (e.g., breathing technique, pressure point mossage)	consequences; urgent intervention indicated Life-threatening consequences Persistent or severe episodes associated with synoope; urgent intervention indicated	Death
iryngoal stenosis elinition: A disorder charact iryngopharyngoal reesthosia elinition: A disorder charact iryngoapaam	diagnosis observations only; intervention not indicated entired by a narrowing of the larger Mild symptoms; no anxiety; intervention not indicated terized by an uncomfortable persis	airway breathing), but causing no respiratory dafresas; medical management indicand (e.g., steroids) geal airway. Moderate symptoms; mild ansiety, but no dyspinas; ahort duration of observation and or ansietyle inclusated; limiting instrumental ADL tent sensation in the area of the Transient optioods; intervertion not indicated muscular contraction of the vocal muscular contraction of the vocal	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms; dyspnea and awallowing difficulty; limiting self care ADL laryngopharyro. Recurrent episodes; ronincaster intervention indicated (e.g., breathing technique, pressure point massage) conds.	consequences; urgent intervention indicated Lite-threatening consequences Persistent or severe episodes associated with synopes; urgent intervention indicated (is-g. Renoptic taryngoscopy, intubation, botox injection)	Death Death
sryngoal stenosis elinition: A disorder charact sryngopharyngoal seathesis elinition: A disorder charact sryngospases	diagnosis observations only; intervention not indicated actual by a narrowing of the large, Mild symptoms; no anxiety, intervention not indicated control by an uncomfortable pensis actual by paroxysmall spasmodic of Radiologic evidence only;	airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids) geal airway. Moderate symptoms; mild anxiety, but no dyspneas; ahort duration of observation and or anxiety/sic indicated; limiting instrumental ADL tent sonsation in the area of the Transient episode; intervention not indicated muscular contraction of the vocal Moderate symptoms; medical Moderate symptoms; medical	endoscopic intervantion indicated (e.g., shart, laser) Severe symptoms; dyspina and awallowing difficulty; limiting self care ADL laryngopharynx. Flocument opisodex; ronlinvasive intervention indicated (e.g., breathing technique, pressure point massage) cords. Transtusion, radiologic,	opnsequences; urgent intervention indicated Life-threatening consequences Persistent or severe episodes associated with symospe; urgent intervention indicated (e.g., fibereptic layingsacepy, intubation, bolox injection)	Death
yngoal etenosis finition: A disorder charact yngopharyngoal codhesia finition: A disorder charact yngospases finition: A disorder charact	diagnosis observations only; intervention not indicated entired by a narrowing of the larger Mild symptoms; no anxiety; intervention not indicated terized by an uncomfortable persis	airway breathing), but causing no respiratory dafresas; medical management indicand (e.g., steroids) geal airway. Moderate symptoms; mild ansiety, but no dyspinas; ahort duration of observation and or ansietyle inclusated; limiting instrumental ADL tent sensation in the area of the Transient optioods; intervertion not indicated muscular contraction of the vocal muscular contraction of the vocal	endoscopic intervention indicated (e.g., shart, laser) Severe symptoms; dyspnea and awallowing difficulty; limiting self care ADL laryngopharyro. Recurrent episodes; ronincaster intervention indicated (e.g., breathing technique, pressure point massage) conds.	consequences; urgent intervention indicated Lite-threatening consequences Persistent or severe episodes associated with synopes; urgent intervention indicated (is-g. Renoptic taryngoscopy, intubation, botox injection)	Death Death

CTCAE 4.03 - June 14, 2010 : Respiratory, thoracic and mediastinal disorders

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CTCAE 4.03 - June 14, 2010 : Respiratory, thoracic and mediastinal disorders





SOMA-LENT 1995 breast

	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORING
Subjective Pain	Occasional & minimal Hypersensation, Pruritus	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	Instructions
Objective Edema Fibrosis* / Fat necrosis Telangiectasia Lymphedema, arm (circumference) Retraction/Atrophy**	Asymptomatic Barely palpable increased density < 1 cm ² 2 cm - 4 cm increase 10% - 25% Epidermal only, ≤ 1 cm ²	Symptomatic Definite increased density and firmness 1 cm ² - 4 cm ² > 4 cm - 6 cm increase > 25% - 40 % Dermal, > 1 cm ²	Secondary dysfunction Very marked density, retraction and fixation > 4 cm ² > 6 cm increase > 40% - 75% Subcutaneous	Useless arm, angiosarcoma Whole breast Bone exposed, necrosis	Score the 12 SOM parameters with 1 - 4 (Score = 0 if there are no toxicities)
Management Pain Edema Lymphedema, arm	Occasional non-narcotic	Regular non-narcotic Elevate arm, elastic stocking	Regular narcotic Medical intervention Compression wrapping, intensive physiotherapy	Surgical intervention Surgical intervention/ mastectomy Surgical intervention/ amputation	Total the scores and divide by 12
Atrophy Ulcer		Medical intervention	Surgical intervention,	Surgical intervention/ mastectomy Surgical intervention/	LENT Score:
		skin according to defined pares as atrophy, retraction or file	wound debridement rameters ** Volume loss de		red to opposite breast) Y/N Date: Y/N Date:
CT/MRI		fat atrophy, and fibrosis den	sity		Y/N Date:



SOMA-LENT 1995 heart



	GRADE 1	GRADE 2	GRADE 3	GRADE 4] :	SCORING
Subjective						2 0 3
Angina pectoris	Occasional, only with intense exertion	With moderate exertion	With mild exertion	At rest	_	Instructions Score the 17 SOM
Pericardial Pain	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	_	parameters with 1 - 4
Palpitation	Occasional	Intermittent	Persistent	Refractory		
Dyspnea	SOB on intense exertion	SOB on mild exertion	SOB at rest, limits all activity	Prevents any physical activity	-	
Pedal edema		Asymptomatic	Symptomatic	Prevents daily activities		
Objective		9				
Pedal edema	1+	2+	3+	4+		(Score = 0 if there are no
Cardiomegaly	Minimal enlargement of cardiosilhouette (ECS)	ECS without pulmonary congestion	ECS with minimal pulmonary congestion	ECS with frank pulmonary edema	-	toxicities)
Cardiac dysrhythmia	Occasional, asymptomatic	Intermittent ECG changes	Persistent ECG changes	Refractory	-	
Myocardial CHF	Asymptomatic decline of resting ejection fraction by ≤20% of baseline	Decline of resting ejection fraction by >20% of baseline	Reversible CHF	Irreversible CHF		Total the
Myocardial ischemia	Abnormal stress test NL resting EKG	Asymptomatic, ST & T wave changes without stress test	Angina without evidence for infarction	Acute myocardial infarction	-	divide by 17
Pericardial disease	Asymptomatic effusion	Rub, chest pain, ECG changes	Tamponade	Constriction	_	
Management				.8		TENE C
Pain (pericarditis)	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Coronary artery bypass	-	LENT Score
Angina	Present but no therapy	Nitroglycerin PRN	Long acting agents	Coronary artery bypass	-	
Pericardial disease	1	Present but no therapy	Pericardiocenthesis	Pericardiectomy		
Cardiac dysrhythmia			Medical intervention	Requires monitoring or cardioversion	-	
Myocardial infarction			Medical intervention	Coronary bypass		
Myocardial CHF	8	7	Medical intervention	Cardiac transplant		

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	GRADE 1	GRADE 2	GRADE 3	GRADE 4	SCORING
Subjective Cough	Occasional	Intermittent	Persistent	Refractory	Instructions Score the 8
Dyspnea	Breathless on intense exertion	Breathless on mild exertion	Breathless at rest, limits all activities	Prevents any physical activity	SOM parameters with 1 - 4
Chest pain/discomfort	Occasional & minimal	Intermittent & tolerable	Persistent & intense	Refractory & excruciating	
Objective					1
Pulmonary fibrosis	Radiological abnormality	Patchy dense abnormalities on radiograph	Dense confluent radiographic changes limited to radiation field	Dense fibrosis, severe scarring & major retraction of normal lung	(Score = 0 if there are no toxicities)
Lung function	10% - 25% reduction of respiration volume and/or diffusion capacity	> 25% - 50% reduction of respiration volume and/or diffusion capacity	> 50% - 75% reduction of respiration volume and/or diffusion capacity	> 75% reduction of respiration volume and/or diffusion capacity	Total the scores and divide by 8
Management					1
Pain	Occasional non-narcotic	Regular non-narcotic	Regular narcotic	Surgical intervention	LENT Score:
Cough		Non-narcotic	Narcotic, intermittent corticosteroids	Respirator, continuous corticosteroids	
Dyspnea	L	Occasional O ₂	Continuous O ₂]
Analytic					
PFT	Decrease to >75% - 90% of preTx value	Decrease to >50% - 75% of preTx value	Decrease to >25% - 50% of preTx value	Decrease to ≤ 25% of preTx value	Y/N Date:
DLCO	Decrease to >75% - 90% of preTx value	Decrease to >50% - 75% of preTx value	Decrease to >25% - 50% of preTx value	Decrease to ≤ 25% of preTx value	Y/N Date:
% O ₂ /CO ₂ saturation	> 70% O ₂ , ≤ 50% CO ₂	> 60% O ₂ , ≤ 60% CO ₂	> 50% O ₂ , ≤ 70% CO ₂	≤50% O ₂ , >70% CO ₂	Y/N Date:
CT/ MRI	Assessment of lung volume	and zones of fibrosis			Y/N Date:
Perfusion scan	Assessment of pulmonary b	blood flow and alveolar fillin	g		Y/N Date:
Lung lavage	Assessment of cells and cyt	tokines			Y/N Date:







REPORTING: IS IT A SOLVED PROBLEM?

Hoeller et al IJROBP 55(4): 1013 (2003)
Normal Tissue

CLINICAL INVESTIGATION

INCREASING THE RATE OF LATE TOXICITY BY CHANGING THE SCORE? A COMPARISON OF RTOG/EORTC AND LENT/SOMA SCORES

Ulrike Hoeller, M.D., Silke Tribius, M.D., Antje Kuhlmey, M.D., Kai Grader, Fabian Fehlauer, M.D., and Winfried Alberti, Ph.D.

1									
()	RI	GI	N	Δ	A	P	TI	CI	D

Berthelet et al Am Journ Clin Oncol 27(6): 626 (2004)

Preliminary Reliability and Validity Testing of a New Skin Toxicity Assessment Tool (STAT) in Breast Cancer Patients Undergoing Radiotherapy

Eric Berthelet, MD,*§ Pauline T. Truong, MDCM,*§ Karin Musso, RN,† Vickie Grant, RTT,† Winkle Kwan, MBBS,*§ Veronika Moravan, MSc,‡ Kelly Patterson, RTT,† and Ivo A. Olivotto, MD*

		m (mage 16.5 / photons The	(Add	ressograph)	
Separation: Treatment Site Energy: Total Dose/frac Shell: Last Chemothe	tion:	Field Size: Technique: Boost: Dose per Fraction: Bolus:		tirchet a het ales socialis depication depication	main a mi mainmai i mainmai i mainmai i i mainmai i main
Date (m/d/y)					
Treatment Day	the second secon				
Intact Skin √-y	es ¢=no				
Erythema	Grading (0=none, 1=faint, transient, 2=bright)				
munon.	Area (cm x cm)	constice (sm)			
Dry Desquamat Area (cm x			19		14
Moist Desquam			6.1 (1.Go	107	27
Exudate: E	Other: O		- 14 Gy	11-16/	16
	• Burning (0-5)		0 dy	1 -01	1 9
Discomfort	Itchiness (0-5)	THE REAL PROPERTY.			
	• Pulling (0-5)		27	I Dec	110
	Tenderness (0-5)	Fields			19
	• Other (0-5)				
Skin Care Treat Fl=Flamazine; NS=NS Soaks; O=Other (species	HC=Hydrocortisone Cream; CS=Cornstarch; G=Glaxal;				
Assessment Tir	me (minutes)	49			
Initials	ACTION AND ADDRESS OF THE PARTY	7 100 100 100	mount of the		



- Which are the organs of interest?
- Which are the informations in QUANTEC for each of these?
- Which are the most important data about these organs?



radiation-related heart



disease (RRHD) → pericarditis, pericardial fibrosis, diffuse myocardial fibrosis, and coronary artery disease (CAD)

heart

• lung

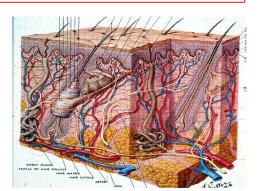
Early → pneumonitis

Late → fibrosis

• skin

Early → dryness, epilation, pigmentation changes, and erythema

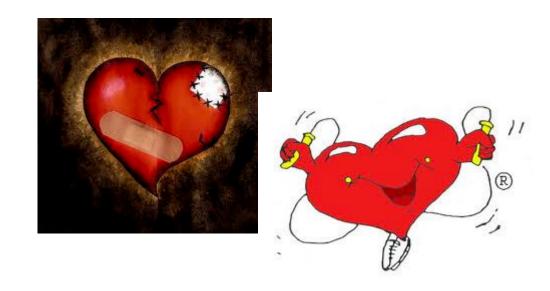
Sub-acute → Dry desquamation



Late → atrophy and fibrosis; pigmentation changes; telangiectasias



Heart



radiation-related heart disease (RRHD) → pericarditis, pericardial fibrosis, diffuse myocardial fibrosis, and coronary artery disease (CAD)





QUANTEC MODEL: heart

Clinical aspects

- Pericardial disease
- Ischemic heart disease → > RR of cardiac morbidity in old series treated with old RT tecniques
- Congestive heart failure
- Valvular disease





QUANTEC MODEL: heart

Clinical aspects

- Pericardial disease
- Ischemic heart disease → > RR of cardiac morbidity in old series treated with old RT tecniques
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- Valvular disease

OAR definition

• challenges in defining volumes (entire heart, pericardium, left ventricle, coronary arteries)



QUANTEC MODEL: heart

Clinical aspects

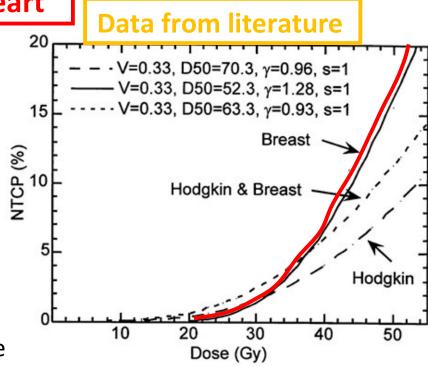
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• challenges in defining volumes (entire heart, pericardium, left ventricle, coronary arteries)

Data about factors affecting the risk and about models used to predict the damage

 damage related to dose and irradiated volumes → minimize the irradiated heart volume





uni S

QUANTEC MODEL: heart

Clinical aspects

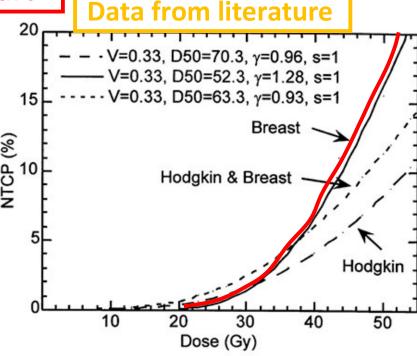
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OAR definition

• challenges in defining volumes (entire heart, pericardium, left ventricle, coronary arteries)

Data about factors affecting the risk and about models used to predict the damage

 damage related to dose and irradiated volumes → minimize the irradiated heart volume



Recommendations about dose/volume

Gagliardi et al IJROBP 76(3) \$77-85 (2010)



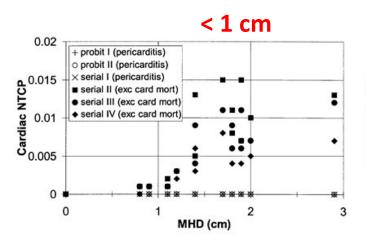


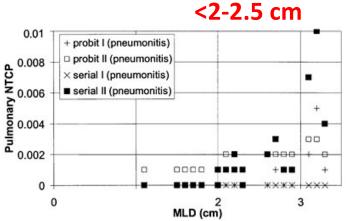
Not only QUANTEC:

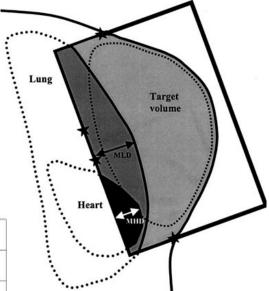
heart

Cardiac and pulmonary doses and complication probabilities in standard and conformal tangential irradiation in conservative management of breast cancer

- Different NTCP model/parameter combinations give different predictions for the risks radiation-induced cardiac and pulmonary morbidity;
- Good agreement when small volumes of OAR were irradiated





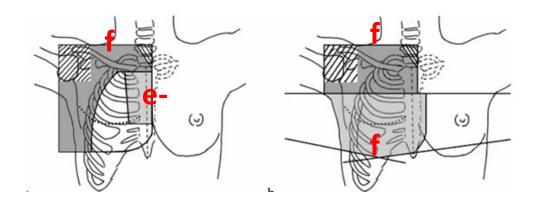


1‰ risk for cardiac and pulmonary morbidity

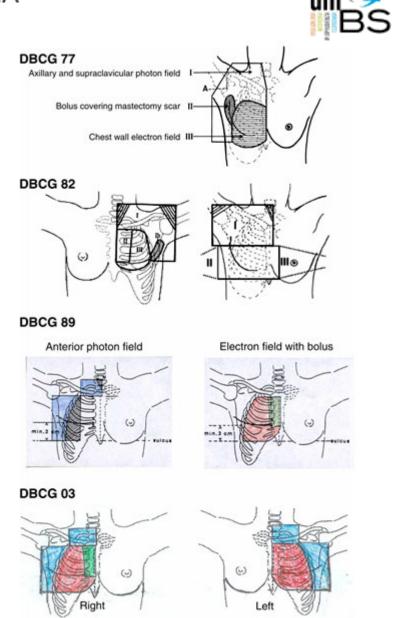


Not only QUANTEC: heart

Strong relation between RT techniques/volumes and doses to OAR



Thomsen Acta Oncol 47: 654 (2008)



M. Overgaard Acta Oncol 47: 639 (2008)





Radiot and Oncol 100: 157 (2011)

Editorial

Radiation-induced heart morbidity after adjuvant radiotherapy of early breast cancer – Is it still an issue?

Birgitte Offersen*, Inger Højris, Marie Overgaard

Department of Oncology, Aarhus University Hospital, Aarhus C, Denmark

Big studies → big biases





Cardiac morbidity

Incidence of heart disease in 35,000 women treated with radiotherapy for breast cancer in Denmark and Sweden Radiot and Oncol 100: 167 (2011)

Paul McGale^a, Sarah C. Darby^{a,*}, Per Hall^b, Jan Adolfsson^c, Nils-Olof Bengtsson^d, Anna M. Bennet^b, Tommy Fornander^e, Bruna Gigante^f, Maj-Britt Jensen^g, Richard Peto^a, Kazem Rahimi^h, Carolyn W. Taylor^a, Marianne Ewertzⁱ

Years since breast cancer diagnosis	Number of events left/right		Incidence ratio, left-sided vs. right-sided (95% CI)	
	al infarction (p=0.7)†		4.	
0-4 5-9	180/139 112/96	<u> </u>	1.21 (0.97-1.51) 1.15 (0.87-1.51)	
10-14	68/54		1.19 (0.87-1.51)	
15+	52/33		1.56 (1.00-2.42)	
Total	412/322	<-	1.22 (1.06-1.42)	
(b) Angina (p=0.06)				
0-4	137/79		1.61 (1.22-2.12)	
5-9	80/76		1.03 (0.75-1.41)	
10-14	38/42	_ _ _	0.86 (0.55-1.34)	
15+	36/25		1.41 (0.84-2.36)	
Total	291/222	<-	1.25 (1.05-1.49)	
(c) Other is chaemic	heart disease (p=0.5)			
0-4	88/72	-	1.13 (0.82-1.54)	
5-9	42/46	_ _ _	0.87 (0.57-1.33)	
10-14	26/32	-	0.77 (0.46-1.29)	
15+	19/18	_	1.19 (0.62-2.31)	
Total	175/168	♦ -	0.99 (0.80-1.23)	
(a+b+c) Ischaemic I	neart disease (p=0.07)		_	
0-4	405/290	/ \	1.30 (1.12-1.51)	hiaaa
5-9	234/218	<u> </u>	1.05 (0.87-1.26)	biases
10-14	132/128	<u>.</u>	0.97 (0.76-1.24)	DIGGES
15+	107/76	T_ =	1.43 (1.06-1.92)	
Total	878/712		1.18 (1.07-1.30)	
(d) Pericarditis (p=0	6)			
0-4	34/19		1.68 (0.96-2.96)	
5-9	19/10		1.92 (0.89-4.13)	
10+	7/7		0.95 (0.33-2.73)	
Total	60/36	$\langle \rangle$	1.61 (1.06-2.43)	
(e) Valvular heart di	sease (n=0.3)			
0-4	39/31	_ _	1.17 (0.73-1.88)	
5-9	22/10		2.37 (1.11-5.05)	
10+	33/19		1.74 (0.99-3.08)	
Total	94/60		1.54 (1.11-2.13)	
(f) Other heart disea	se (n=0.7)			
0-4	514/496		0.97 (0.85-1.09)	
5-9	352/337	I.	1.00 (0.86-1.16)	
10-14	198/207	4	0.93 (0.77-1.13)	
15+	179/168	7	1.11 (0.90-1.37)	
Total	1243/1208		0.99 (0.91-1.07)	
(a-f) All heart diseas	se (p=0.2)			
0-4	992/836	/ • \	1.11 (1.01-1.21)	
5-9	627/575	/ - \	1.06 (0.94-1.18)	
10-14	347/346	4	0.96 (0.83-1.12)	
15+	309/259	\ T = -/	1.23 (1.04-1.45)	
Total	2275/2016	\ b /	1.08 (1.02-1.15)	
i Otal	22/3/2010			
		0.0 1.0 2.0 3.)	
	Reduced inci	dence Increased in	cidence	

Characteristic	Percentage given radiotherapy		Number of	
	Left-sided breast cancer	Right-sided breast cancer	women	
Country				
Denmark	42	42	43,802	
Sweden	58	58	28,332	
Year of breast cancer diagnosis	•			
1976-1989	43	44	27,898	
1990-2006	51	51	44,236	
Age at breast cancer diagnosis (vears)			
<50	56	56	18,689	
50-59	51	52	20,046	
60-69	45	45	19,899	
70-79	39	39	13,500	
Breast-conserving surgery				
Yes	93	93	18.654	
No/unknown†	33	33	53,480	
Hormonal therapy				
Yes	56	56	22,427	
No/unknown	44	45	49,707	
Chemotherapy				
Yes	59	60	13,747	
No/unknown	46	46	58,387	
Ischaemic heart disease prior to	breast cancer:			
Yes	35	40	1766 [§]	
No/unknown	48	49	70,368	
Other heart disease prior to bre	ast cancer			
Yes	39	39	2413	
No/unknown	48	49	69,721	
Totals				
Percentage given radiotherapy	48	49	48	
Number of women	37,269	34,865	72,134	





Cardiac morbidity

Incidence of heart disease in 35,000 women treated with radiotherapy for breast cancer in Denmark and Sweden Radiot and Oncol 100: 167 (2011)

Paul McGale^a, Sarah C. Darby^{a,*}, Per Hall^b, Jan Adolfsson^c, Nils-Olof Bengtsson^d, Anna M. Bennet^b, Tommy Fornander^e, Bruna Gigante^f, Maj-Britt Jensen^g, Richard Peto^a, Kazem Rahimi^h, Carolyn W. Taylor^a, Marianne Ewertzⁱ

Years since breast cancer	Number of events		Incidence ratio, left-sided vs.		Characteristic	Percentage given radiotherapy		Number of
(a) Acute myocardial	left/right nfarction (p=0.7)† 180/139		right-sided (95% CI)			Left-sided breast cancer	Right-sided breast cancer	women
5-9 10-14	112/96 68/54	1	1.15 (0.87-1.51) 1.19 (0.83-1.70)		Country			
15+ Total	52/33 412/322		1.56 (1.00-2.42) 1.22 (1.06-1.42)		Denmark	42	42	43,802
	412/322	ľ	1.22 (1.00 1.72)		Sweden	58	58	28,332
(b) Angina (p=0.06) 0-4	137/79		1.61 (1.22-2.12)		Year of breast cancer diagnosis			
5-9 10-14	80/76 38/42		1.03 (0.75-1.41)		rear of theast cancer diagnosis	43	44	27,898
15+ Total	36/25 291/222				_	51	51	44,230
(c) Other ischaemic h		ľ	«Deaths fr	nm ha	art			,
0-4	88/72	<u>-</u>	"Deaths II		gnosis		50	10.000
5-9 10-14	42/46 26/32	<u>-</u>				56 51	56 52	18,689 20.046
15+ Total	19/18 175/168	-	disease wa	sa lawa	or l	45	52 45	19,899
(a+b+c) Ischaemic he			uisease wa	do IOW	er I	39	39	13,500
Ò-4	405/290	/ [-				39	39	13,300
5-9 10-14	234/218 132/128	#	-1 -1	•	ery			
15+ Total	107/76 878/712	- ■-	than the n	umbei	r	93	93	18,654
			© CHAIL CITC HAILIBCI 33 33 53,480					
(d) Pericarditis (p=0.6 0-4	34/19	\sim		_				
5-9 10+	19/10 7/7	_	avpacted f	rom		56	56	22,427
Total	60/36	<	expected f	10111		44	45	49,707
(e) Valvular heart dise			•					
0-4 5-9	39/31 22/10	—	4 ! 1 - 1			59	60	13,747
10+ Total	33/19 94/60		national de	eatns	rates»	46	46	58,387
(f) Other heart disease			mational a	Catilo			40	30,307
0-4	514/496	, t	0.97 (0.65-1.09)			o breast cancer:		
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15+ Total	179/168 1243/1208	<u></u>	1.11 (0.90-1.37) 0.99 (0.91-1.07)		No/unknown	48	49	70,368
			0.55 (0.51-1.01)		Other heart disease prior to be	east cancer		
(a-f) All heart disease 0-4	992/836	/ - \	1.11 (1.01-1.21)		Yes	39	39	2413
5-9 10-14	627/575 347/346		1.06 (0.94-1.18) 0.96 (0.83-1.12)		No/unknown	48	49	69,721
15+	309/259	\ - /	1.23 (1.04-1.45) 1.08 (1.02-1.15)					
Total	2275/2016		1.00 (1.02-1.10)		Totals			
		\top			Percentage given radiotherapy		49	48
			2.0 3.0		Number of women	37,269	34,865	72,134
	Reduced incid	ence inc	reased incidence					





Editorial

Radiation-induced heart morbidity after adjuvant radiotherapy of early breast cancer – Is it still an issue?

Birgitte Offersen*, Inger Højris, Marie Overgaard

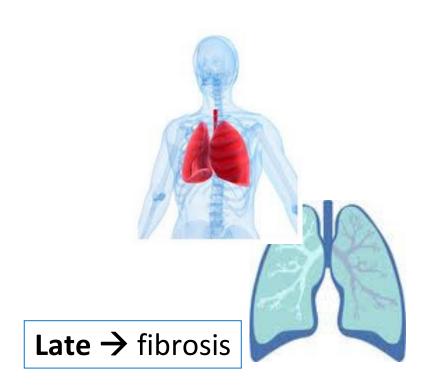
Department of Oncology, Aarhus University Hospital, Aarhus C, Denmark

Aspect	Factors and unsolved issues of importance				
Patient related	Age Long expected life-time Co-morbidities: connective tissue disease, hypertension, diabetes mellitus a.o. Systemic therapy may have negative influences on the heart: anthracyclines, trastuzumab, taxanes, tamoxifen, letrozole Risk that the systemic therapy potentiates the radiation effects on the heart Alcohol and tobacco Individual sensitivity to late heart morbidity Hereditary heart disease				
Planning related	Irradiated volume of the heart Are some structures of the heart more sensitive to RT than others? Is the heart always a serial organ? Total dose and fractionation, boost Patient position during radiotherapy (prone/supine) Presence of hot spots in the heart				
Technique related	Relevant organ at risk definition (what is relevant to delineate: heart, pericardium, some or all coronary vessels, valves). How to delineate this? What to report? Maximum or mean, V5, V10, V20? Inaccuracy in reporting doses due to different TPS and daily set up variation				
Endpoint related	What heart morbidity is it relevant to look for? Is it possible to distinguish between radiation-induced heart disease and other far more frequent heart morbidities? How to measure the morbidity? Is it relevant to look for sub-clinical heart disease? For how long should the patient be evaluated, is it lifelong?				
Ethical related	Is it acceptable to induce a fear of heart disease of around 1% absolute increased risk in a cancer patient? It is now technically feasible to (almost) avoid dose to the heart, so is a non-gated therapy for left-sided breast cancer no longer acceptable?				
Society related	Is it cost-effective to set up screening programs to find those patients who may develop late radiation induced heart disease?				



Lung

Early → pneumonitis







QUANTEC MODEL: lung

Clinical aspects

- Radiation clinical pneumonitis (RP) in 1-5
 % of patients irradiated for breast
- endpoints: symptoms; radiologic alterations; pulmonary function





Not only QUANTEC: lung

PULMONARY CHANGES AFTER RADIOTHERAPY FOR CONSERVATIVE TREATMENT OF BREAST CANCER: A PROSPECTIVE STUDY

Marco Krengli, M.D.,* Mariano Sacco, M.D.,[†] Gianfranco Loi, Ph.D.,[‡] Laura Masini, M.D.,* Daniela Ferrante, M.D.,[§] Giuseppina Gambaro, M.D.,* Marco Ronco, M.D.,[¶] Corrado Magnani, M.D.,[§] and Alessandro Carriero, M.D.,[†]

Grade	Before RT	3 mo after RT	9 mo after RT
0	41 (100)	9 (22.0)	9 (22.0)
1	0 (0)	19 (46.3)	24 (58.5)
2	0 (0)	10 (24.4)	8 (19.5)
3	0 (0)	3 (7.3)	0 (0)

88% of the case have G1-3 radiological evidence of damage → 4.9% had symptoms of G1 RP

Table 3. Mean lung volume receiving >25 Gy and corresponding grade of lung changes scored using classification of Wishioka et al. (18) at 3 and 9 months

	3-mo Assessment		9-mo Assessment		
Grade	Lung volume*	Proportion of lung volume	Lung volume*	Proportion of lung volume	
0	67.8 (39.2)	0.05 (0.02)	70.4 (33.5)	0.05 (0.02)	
1	86.0 (44.8)	0.07 (0.03)	92.6 (48.3)	0.07 (0.03)	
2	131.9 (38.7)	0.10 (0.03)	147.5 (38.1)	0.11 (0.03)	
3	157.6 (50.5)	0.10 (0.01)	_	_	





QUANTEC MODEL: lung

Clinical aspects

- Radiation clinical pneumonitis (RP) in 1-5
 % of patients irradiated for breast
- endpoints: symptoms; radiologic alterations; pulmonary function

Data about factors affecting the risk and about models used to predict the damage

- NTCP: mean lung dose (MLD) model →
 ...a variety of dose levels are predictive of
 RP suggests that there is no DOSE
 THRESHOLD below which there is no risk
- "acceptable" risk level varies with the clinical scenario





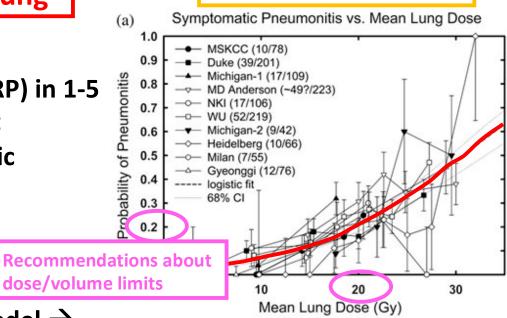
QUANTEC MODEL: lung

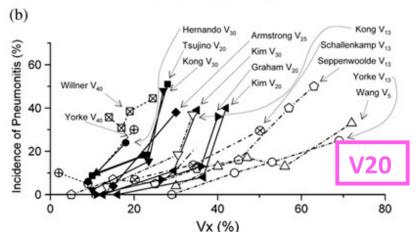
Clinical aspects

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- NTCP: mean lung dose (MLD) model →
 ...a variety of dose levels are predictive of
 RP suggests that there is no DOSE
 THRESHOLD below which there is no risk
- "acceptable" risk level varies with the clinical scenario





Marks et al IJROBP 76(3) S70-76 (2010)





Skin – Soft tissues

Early → dryness, epilation, pigmentation changes, and erythema

Sub-acute → Dry desquamation

Late
→atrophy and fibrosis; pigmentation changes; telangiectasias



QUANTEC MODEL: skin → does not exist

- It is a problem ← cosmetic outcome ← discomfort
 - limit daily activities
 - breaks from treatm.

Factors related to skin toxicity

- factors different from RT as age, smoking, diabetes, others intrinsic factors
- total dose: in excess to 50 Gy to whole breast
- dose per fraction: not definitive results
- dose inhomogeneity → "double thuble" (hot spots created within inhomogeneous dose distribution total dose and dose per fraction)
- systemic treatment





QUANTEC MODEL: skin→ does not

exist

It is still a problem? ←> cosmetic outcome ←> - discomfort

« Previous

International Journal of Radiation Oncology * Biology * Physics

Volume 81, Issue 2 , Pages 397-402, 1 October 2011

ily activities rom treatm.

Comparison of Provider-Assessed and Patient-Reported Outcome Measures of Acute Skin Toxicity During a Phase III Trial of Mometasone Cream Versus Placebo During Breast Radiotherapy: The North Central Cancer Treatment Group (No6C4)

col 17(5): 22 (2010)

COLOGY

Michelle A. Neben-Wittich, M.D., Pamela J. Atherton, M.S., David J. Schwartz, M.D., Jeff A. Sloan, Ph.D., Patricia C. Griffin, M.D., Richard L. Deming, M.D., Jon C. Anders, M.D., Charles L. Loprinzi, M.D., Kelli N. Burger, B.S., James A. Martenson, M.D., Robert C. Miller, M.D.

herapy apy do

toxicity in breast cancer

Miao-Fen Chen^{1,2*}, Wen-Cheng Chen^{1,2}, Chia-Hsuan La



not increase radiation-induced dermatitis in breast cancer patients

T. Hijal MD, * A.A. Al Hamad MD, † T. Niazi MD, † K. Sultanem MD, † B. Bahoric MD, † T. Vuong MD, † and T. Muanza MD, †











An accurate toxicity evaluation is mandatory:

- To *correlate* and *confirm (or not)* the data derived from theoretical mathematical models (e.g., a/B ratio) with adequate clinical data
- To collect data to guide therapeutic decisions

• To *compare* the effectiveness and toxicities of the different treatment options





Heart

QUANTEC

Lung

9. FUTURE TOXICITY STUDIES

Improved toxicity prediction requires prospective clinical trials based on 3D dosimetric data and careful long-term follow-up of patients who have received potentially cardiotoxic chemotherapy and RT. Prospective cardiac mortality studies are unlikely to be numerous. Hopefully, the few existing dose-volume predictors for cardiac mortality will be modified by new retrospective analyses based on larger data

9. FUTURE TOXICITY STUDIES

Progress regarding the predictors of RT-induced lung injury requires further understanding of the followin-

Endpoint interaction

Impact of an in situ lung cancer on the risk of radiationinduced lung injury

The data for whole-lung radiation is derived essentially The study of RT-induced lung injury is confount from patients without primary lung cancers (e.g., elective

Key words:

- prospective clinical trials
- ✓ clear identification of end-point
- correlation of dosimetric informations with the clinic
- √ correlation of end-point dosimetric information clinical informations - biological informations

- c) Future studies should incorporate baseline cardiovascular risk factors, such as the Framingham or Reynolds score (33-35). This will allow consideration of potential interactive effects between RT and traditional cardiac risk factors.
- d) Additional work is needed to understand the impact of hypofractionated radiation regimens on the heart.
- e) A deeper understanding of the global physiological effects of thoracic RT is needed (e.g., interactions between the heart and lung irradiation, as suggested in some animal studies) (63).

RT was related to the volume of lung and heart (38-40).

combined with the acute toxicities of amifostine (nausea/vomiting, hypotension, infection, and rash), have dissuaded many from using it in routine practice. One small randomized study demonstrated a protective effect of pentoxifylline, but pentoxifylline is not currently used in routine clinical practice (45).

Biomarkers

Additional work is needed to assess the predictive ability offered by biomarkers (see Bentzen et al. in this issue), such as transforming growth factor β (measured before and/or during RT) (46).