



Radiochirurgia e Radioterapia stereotassica: non solo tecnica



CONVEGNO DEL GRUPPO REGIONALE PIEMONTE-LIGURIA-VALLE D'AOSTA

Nuovi constraints di dose

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TOLERANCE OF NORMAL TISSUE TO THERAPEUTIC IRRADIATION

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- 1991
- Pre 3DCRT
- Volume effect (1/2-1/3-whole organ)

Table 1. Normal tissue tolerance to therapeutic irradiation

Organ	TD 5/5 Volume			TD 50/5 Volume			Selected endpoint
	1/3	2/3	3/3	1/3	2/3	3/3	
Kidney I	5000	3000*	2300	—	4000*	2800	Clinical nephritis
Kidney II							
Bladder	N/A	8000	6500	N/A	8500	8000	Symptomatic bladder contracture and volume loss
Bone:							
Femoral Head I and II	—	—	5200	—	—	6500	Necrosis
T-M joint mandible	6500	6000	6000	7700	7200	7200	Marked limitation of joint function
Rib cage	5000	—	—	6500	—	—	Pathologic fracture
Skin	10 cm ²	30 cm ²	100 cm ²	10 cm ²	30 cm ²	100 cm ²	Telangiectasia
	7000	6000	5500	—	—	7000	Necrosis
Brain	6000	5000	4500	7500	6500	6000	Ulceration
Brain stem	6000	5300	5000	—	—	6500	Necrosis
Optic nerve I & II	No partial volume	—	5000	—	—	6500	Infarction
Chiasma	No partial volume	—	5000	No partial volume	—	6500	Necrosis
Spinal cord	5 cm	10 cm	20 cm	5 cm	10 cm	20 cm	Infarction
	5000	5000	4700	7000	7000	7000	Necrosis
Cauda equina	No volume effect	—	6000	No volume effect	—	7500	Infarction
Brachial plexus	6200	6100	6000	7700	7600	7500	Necrosis
Eye lens I and II	No partial volume	—	1000	—	—	1800	Ulceration
Eye retina I and II	No partial volume	—	4500	—	—	6500	Necrosis
Ear mid/external	3000	3000	3000*	4000	4000	4000*	Infarction
Ear mid/external	5500	5500	5500*	6500	6500	6500*	Necrosis
Parotid* I and II	—	3200*	3200*	—	4600*	4600*	Ulceration
				(TD 100/5 is 5000)			Necrosis
Larynx	7900*	7000*	7000*	9000*	8000*	8000*	Infarction
Larynx	—	4500	4500*	—	—	8000*	Necrosis
Lung I	4500	3000	1750	6500	4000	2450	Infarction
Lung II							Necrosis
Heart	6000	4500	4000	7000	5500	5000	Ulceration
Esophagus	6000	5800	5500	7200	7000	6800	Necrosis
Stomach	6000	5500	5000	7000	6700	6500	Ulceration
Small intestine	5000	—	4000*	6000	—	5500	perforation
Colon	5500	—	4500	6500	—	5500	perforation
Rectum	Volume 100 cm ³	—	6000	Volume 100 cm ³	—	8000	perforation
	No volume effect	—	—	No volume effect	—	—	perforation
Liver	5000	3500	3000	5500	4500	4000	perforation

* < 50% of volume doesn't make a significant change.

QUANTEC:



Organ	Volume segmented	Irradiation type (Partial organ unless otherwise stated) [*]	Endpoint	Dose (Gy), or dose/volume parameters [*]		Rate (%)	Notes on dose/volume parameters
Brain	Whole organ	3D-CRT	Symptomatic necrosis	Dmax	< 60	< 3	Data at 72 and 90 Gy extrapolated from BED models.
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax	72	5	
	Whole organ	3D-CRT	Symptomatic necrosis	Dmax	90	10	
	Whole organ	SRS (single fraction)	Symptomatic necrosis	V12	< 5-10 cc	< 20	Rapid rise when V12 > 5-10 cc
Brain stem	Whole organ	Whole organ	Permanent cranial neuropathy or necrosis	Dmax	< 54	< 5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	D1-10cc ^{****}	≤ 59	< 5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	Dmax	< 64	< 5	Point dose << 1 cc
	Whole organ	SRS (single fraction)	Permanent cranial neuropathy or necrosis	Dmax	< 12.5	< 5	For patients with acoustic tumors
Optic nerve / chiasm	Whole organ	3D-CRT	Optic neuropathy	Dmax	< 55	< 3	Given the small size, 3D CRT is often whole organ#
	Whole organ	3D-CRT	Optic neuropathy	Dmax	= 55-60	3-7	
	Whole organ	3D-CRT	Optic neuropathy	Dmax	> 60	> 7-20	

But SBRT before

- protocols
- QUANTEC
- Report of AAPM Task Group 101

Dose tolerance guidelines were extremely rare

-> we began to accumulate sparsely published data



It grew to 500 dose tolerance limits and as of 2016 over 1000 published limits but

- Discordant
- Ever changing
- Lack quantitative estimates of corresponding incidence of complication

- NTCP for SBRT are considerably different from conventional RT due to extreme dose fractionation schemes
- Normal tissue dose limits for SBRT should not be directly extrapolated from conventional RT data
- Attention to fraction size, total dose, time intrafractions, OTT

Dose Tolerance for Stereotactic Body Radiation Therapy



- **NTCP for SBRT!**

few published dose-response models to evaluate. The selection criteria for this issue of Seminars, therefore, are the complete opposite: each of these articles after the introduction presents new data and dose-response modeling from an institution, for a critical structure that previously did not have many published dose-response models for SBRT, or where an additional new model could supplement the information that had been sparse. We hope that both projects provide enduring value to the field.

Dose tolerance limit

Human dose tolerance to RT depends on many factors but must specify at least:

- Dose
- Fractionation
- Volume
- Endpoint
- Follow up
- Estimated risk of the endpoint occurring within the follow up time



Endpoint and length of follow up must be clearly stated

Emami 5 years -> convenient, both early and late toxicity but for SBRT.....

- No much available data yet
- Interest in timing of the onset of symptoms

DVH Risk Map:

Seminars in
**RADIATION
ONCOLOGY**

Introduction and Clinical Overview of the DVH Risk Map

Sucha O. Asbell, MD,^{*} Jimm Grimm, PhD,[†] Jinyu Xue, PhD,^{*}
Meng-Sang Chew, PhD,[‡] and Tamara A. LaCouture, MD^{*}

- Simple graph
 - > information relating a range of dose tolerance limits as a function of the number of fractions
 - > help physicians make decisions
- Show the state of the literature for each critical structure

Low risk – high risk:

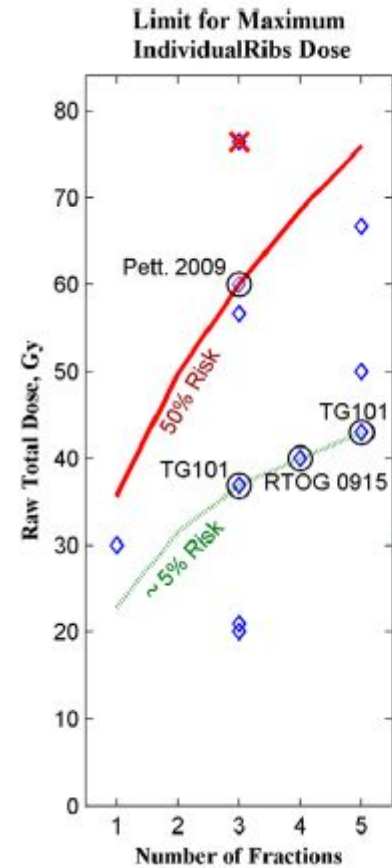
EMAMI: 5% and 50% risk levels

but some structures (spinal cord) required much lower complications rate than others structures as ribs.

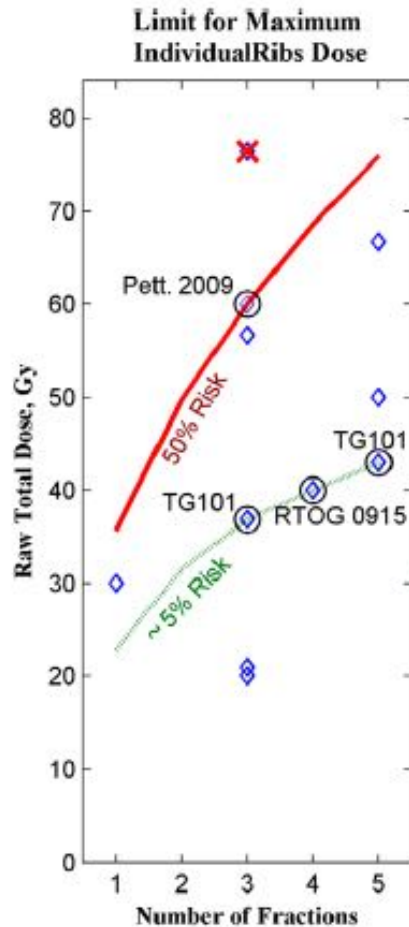
compromise



QUANTEC: custom risk levels for each structure



- Includes a plot of all published dose tolerance limits in 1-5 fractions -> the highest commonly used limit is selected as the high risk limit
- Low risk limit



	Low-Risk Limit (~5%)	High-Risk Limit (~50%)
Number Of Fractions	Dmax Limit (Gy)	Dmax Limit (Gy)
3 fx	36.9 Gy (ref 41), 4.5% Risk	60 Gy (ref 58), 49.9% Risk
4 fx	40.0 Gy (ref 39), 3.9% Risk	
5 fx	43.0 Gy (ref 41)	

The risk level of each of these limits can be determined from a dose response model, that is an equation that gives risk as a function of dose

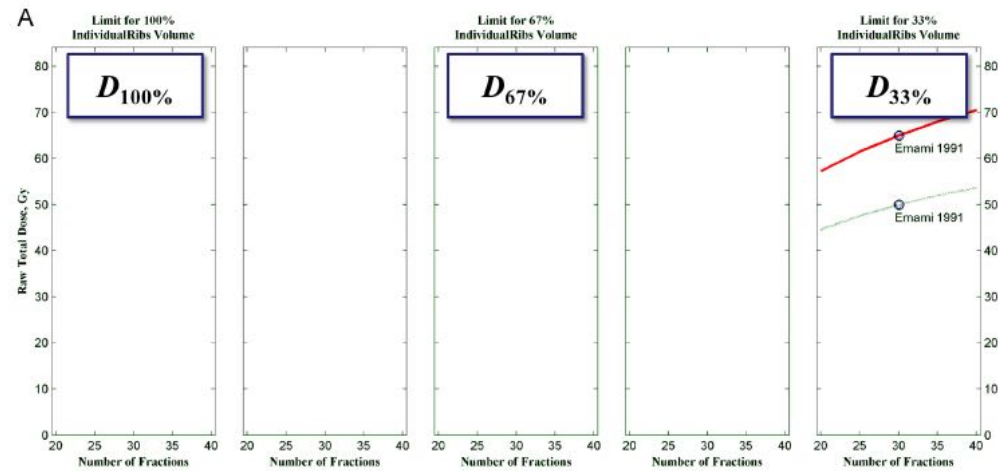
✧ each published limit

✖ published complications for which there is insufficient data to know if it is an acceptable risk level

Volume effects:

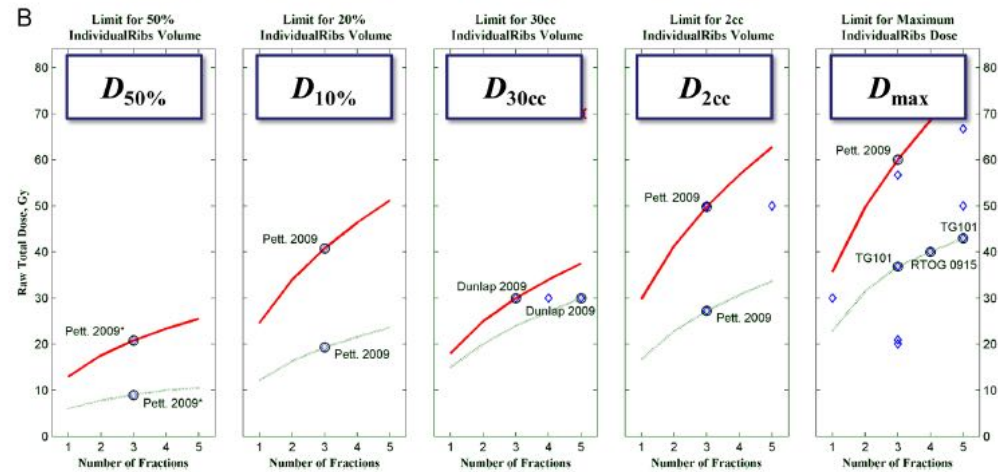
1- Conventional fractionation

EMAMI: dose tolerance limits for large volumes

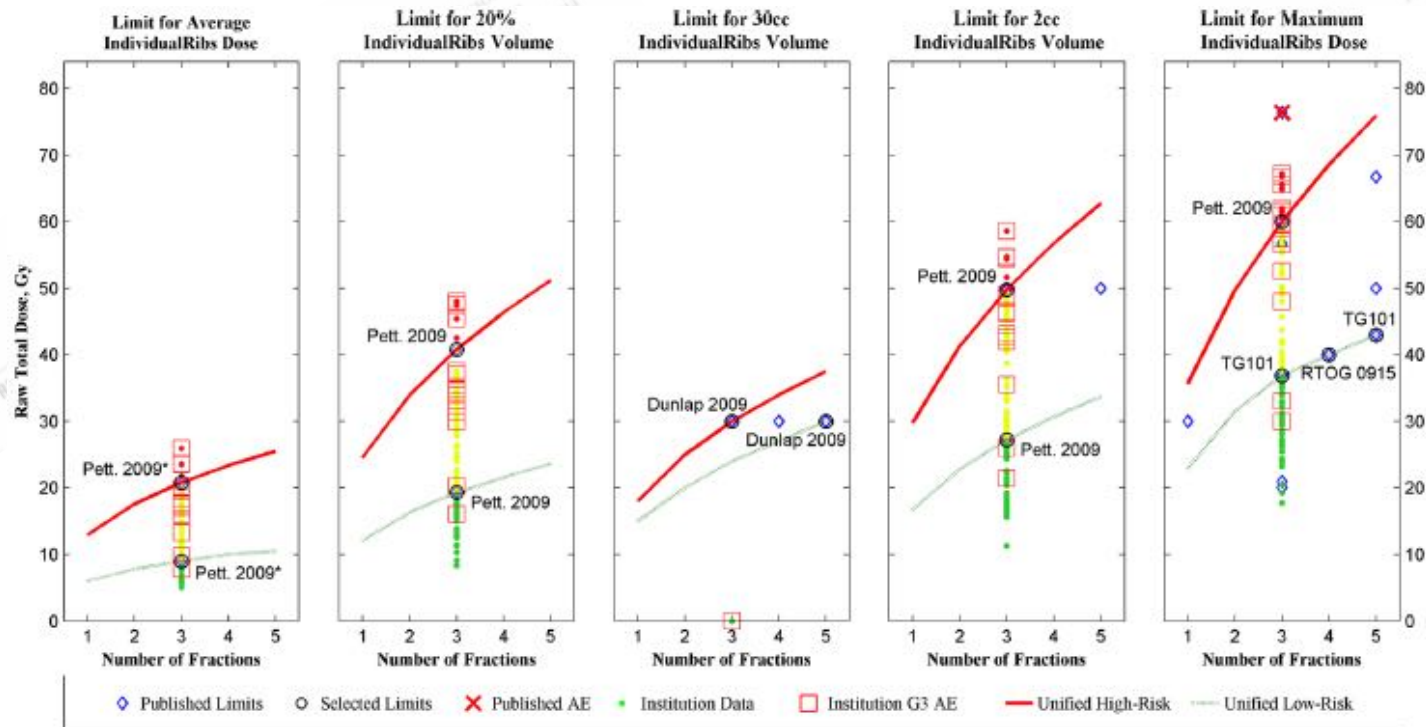


2- SBRT

Smaller volumes
Absolute volumes ->
Specific to each
anatomical structure

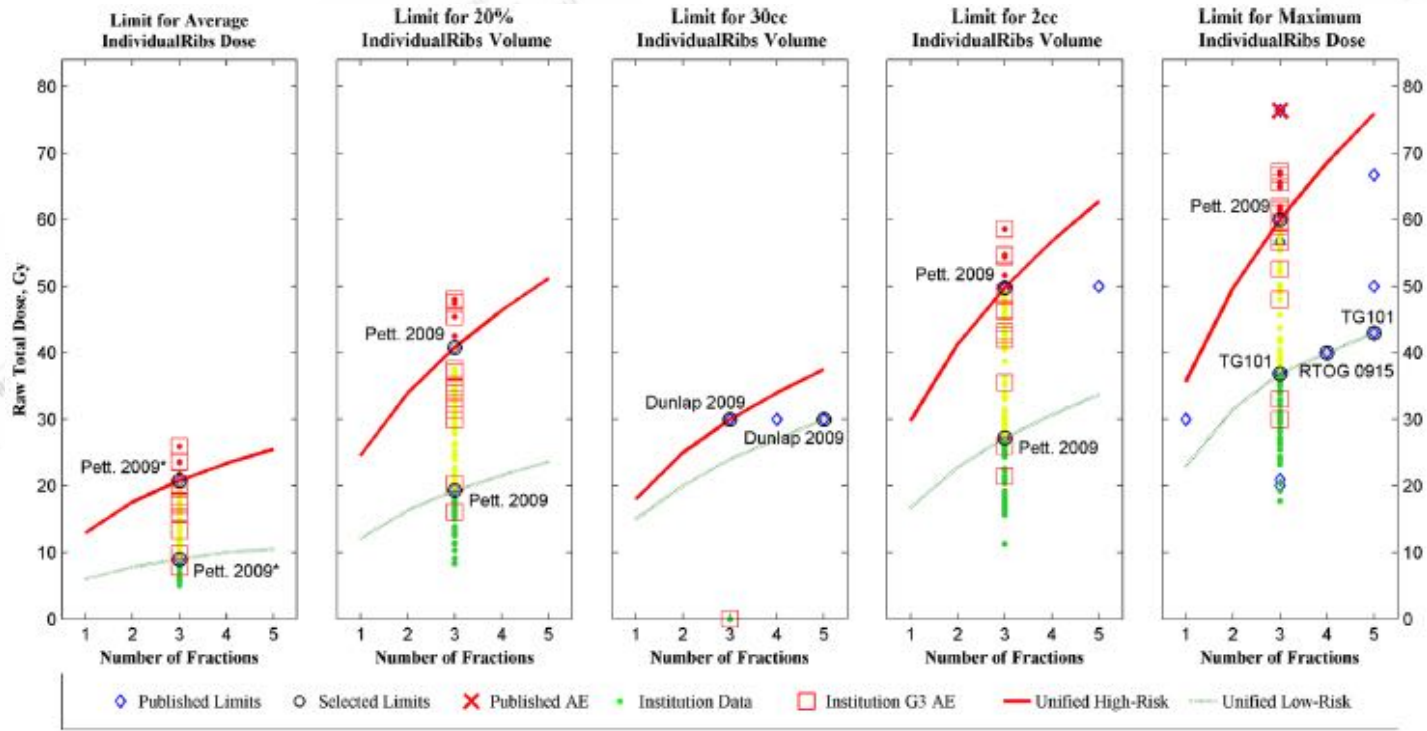


DVH Risk map for ribs:



Endpoint: RT induced rib fractures G1 up to G3-4

- dose volume points below low risk limits
- dose volume points above high risk limits
- dose volume points between low and high risk limits



	Low Risk Limits					High Risk Limits				
	Dmean Limit (Gy)	D20% Limit (Gy)	D30cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)	Dmean Limit (Gy)	D20% Limit (Gy)	D30cc Limit (Gy)	D2cc Limit (Gy)	Dmax Limit (Gy)
1 fx	6.0	12.1	15.0	16.7	22.9	12.9	24.6	18.0	29.8	35.7
2 fx	7.8, 5.0%	16.3, 5.0%	20.0	22.8, 5.0%	31.5, 5.0%	17.6, 50.0%	33.9, 50.0%	25.0	41.3, 50.0%	49.7, 50.0%
3 fx	9.0, 5.0%	19.3, 5.0%	24.0	27.2, 5.0%	36.9, 4.5%	20.8, 50.0%	40.8, 50.0%	30.0	49.8, 50.0%	60.0, 49.9%
4 fx	10.0, 5.1%	21.6, 5.0%	27.0	30.7, 5.0%	40.0, 3.9%	23.4, 50.0%	46.4, 50.0%	34.0	56.8, 50.0%	68.6, 50.0%
5 fx	10.5	23.6	30.0	33.7	43.0	25.5	51.2	37.5	62.8	76.0



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Normal Tissue Tolerance in Stereotactic Body Radiation Therapy

Edited by Jimm Grimm

- Dose-Response Modeling of the Visual Pathway Tolerance to Single-Fraction and Hypofractionated Stereotactic Radiosurgery** Review Article
Pages 97-104
Susan M. Hiniker, Leslie A. Modlin, Clara Y. Choi, Banu Atalar, Kira Seiger, Michael S. Binkley, Jeremy P. Harris, Yaping Joyce Liao, Nancy Fischbein, Lei Wang, Anthony Ho, Anthony Lo, Steven D. Chang, Griffith R. Harsh, Iris C. Gibbs, Steven L. Hancock, Gordon Li, John R. Adler, Scott G. Soltys
▶ Abstract | PDF (1000 K) | Supplementary content
- Multisession Radiosurgery for Hearing Preservation** Review Article
Pages 105-111
Abdul Rashid, Sana D. Karam, Beenish Rashid, Jeffrey H. Kim, Dalong Pang, Walter Jean, Jimm Grimm, Sean P. Collins
▶ Abstract | PDF (936 K)
- Toxicities Following Stereotactic Ablative Radiotherapy Treatment of Locally-Recurrent and Previously Irradiated Head and Neck Squamous Cell Carcinoma** Review Article
Pages 112-119
Kimmen Quan, Karen M. Xu, Yongqian Zhang, David A. Clump, John C. Flickinger, Ron Lalonde, Steven A. Burton, Dwight E. Heron
▶ Abstract | PDF (348 K)
- Esophageal Dose Tolerance in Patients Treated With Stereotactic Body Radiation Therapy** Review Article
Pages 120-128
Joost J. Nuyttens, Vitali Moiseenko, Mark McLaughlin, Sheena Jain, Scott Herbert, Jimm Grimm
▶ Abstract | PDF (984 K)
- Dose-Response Model for Chest Wall Tolerance of Stereotactic Body Radiation Therapy** Review Article
Pages 129-134
Frank Kimsey, Jesse McKay, Jeffrey Gefter, Michael T. Milano, Vitali Moiseenko, Jimm Grimm, Ronald Berg
- Validity of Current Stereotactic Body Radiation Therapy Dose Constraints for Aorta and Major Vessels** Review Article
Pages 135-139
Jinyu Xue, Gregory Kubicek, Ashish Patel, Benjamin Goldsmith, Sucha O. Asbell, Tamara A. LaCouture
▶ Abstract | PDF (1499 K) | Supplementary content
- Dose and Volume of the Irradiated Main Bronchi and Related Side Effects in the Treatment of Central Lung Tumors With Stereotactic Radiotherapy** Review Article
Pages 140-148
Marloes Duijm, W. Schillemans, Joachim G. Aerts, B. Heijmen, Joost J. Nuyttens
▶ Abstract | PDF (1860 K)
- Dose-Volume Histogram Analysis of Stereotactic Body Radiotherapy Treatment of Pancreatic Cancer: A Focus on Duodenal Dose Constraints** Review Article
Pages 149-156
Christy Goldsmith, Patricia Price, Timothy Cross, Sheila Loughlin, Ian Cowley, Nicholas Plowman
▶ Abstract | PDF (1034 K) | Supplementary content
- Small Bowel Dose Tolerance for Stereotactic Body Radiation Therapy** Review Article
Pages 157-164
Tamara A. LaCouture, Jinyu Xue, Gopal Subedi, Qianyi Xu, Justin T. Lee, Gregory Kubicek, Sucha O. Asbell
▶ Abstract | PDF (1270 K) | Supplementary content
- Estimated Risk Level of Unified Stereotactic Body Radiation Therapy Dose Tolerance Limits for Spinal Cord** Review Article
Pages 165-171
Jimm Grimm, Arjun Sahgal, Scott G. Soltys, Gary Luxton, Ashish Patel, Scott Herbert, Jinyu Xue, Lijun Ma, Ellen Yorke, John R. Adler, Iris C. Gibbs
▶ Abstract | PDF (1347 K) | Supplementary content

Conclusions:

DVH risk map ->

- important information in relation to the choice of the fractionation and volume effect
- allow an immediate estimate of the risk



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quali effetti sui tessuti sani, come cambiano i vincoli di dose

Autori: P. Ciammella, G. Mantello, E. D'Angelo.

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