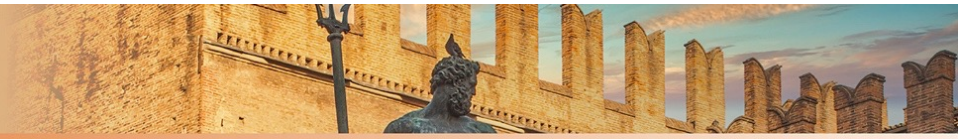
Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia



DICHIARAZIONE

Relatore: FEDERICO GAGLIARDI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario**(NIENTE DA DICHIARARE)**
- Partecipazione ad Advisory Board **(NIENTE DA DICHIARARE)**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

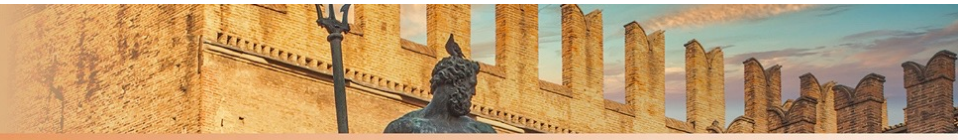
Ritorno al futuro: prospettive per la radioterapia non oncologica (NORT)

Dr. Federico Gagliardi

Università degli Studi della Campania *Luigi Vanvitelli*

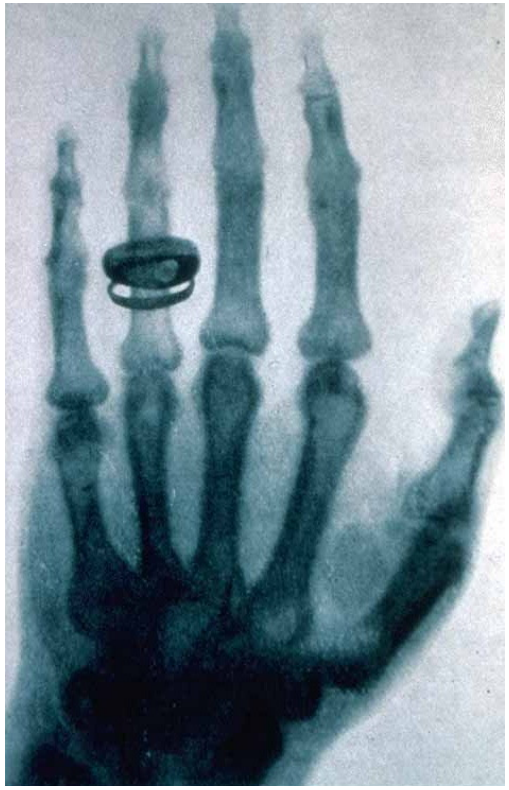
Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia



Associazione Italiana
Radioterapia e Oncologia clinica

BACKGROUND

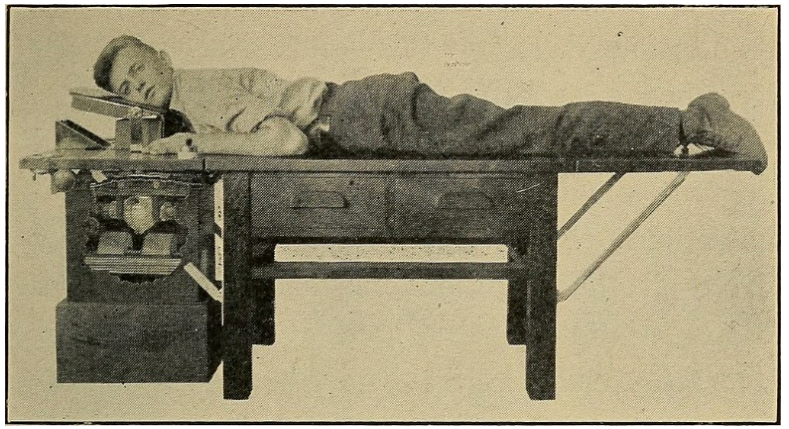


Hand of
Roentgen's wife 1895

BACKGROUND

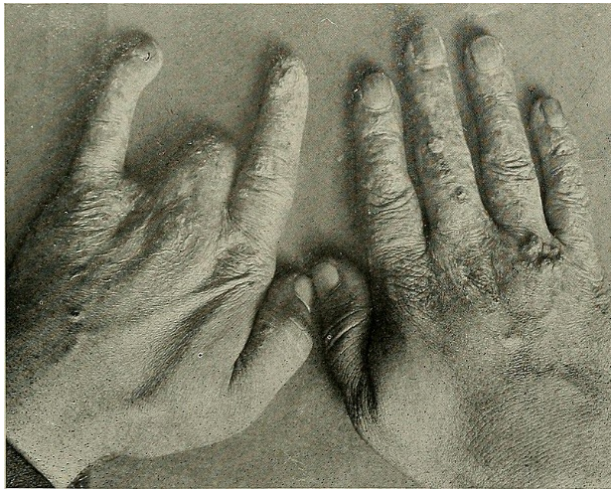
Pedoskop(1930)

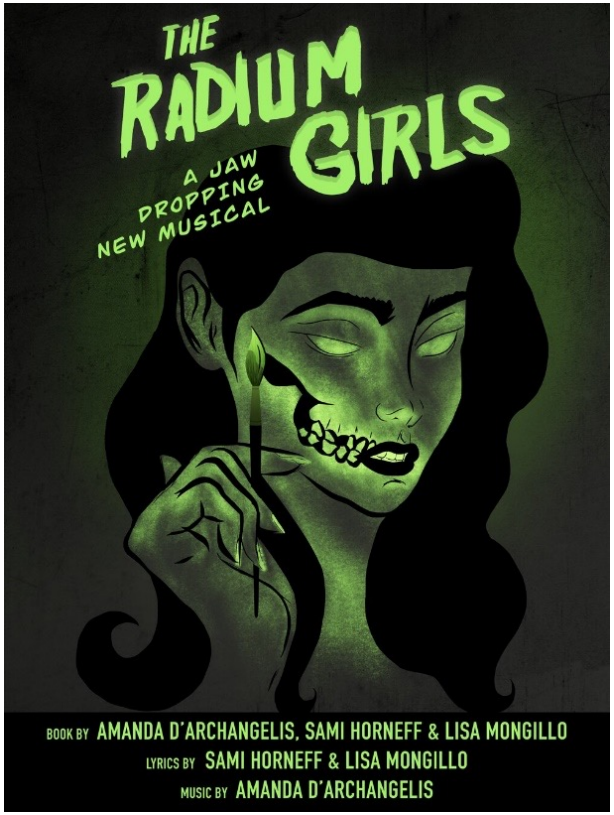
Radithor(1918)



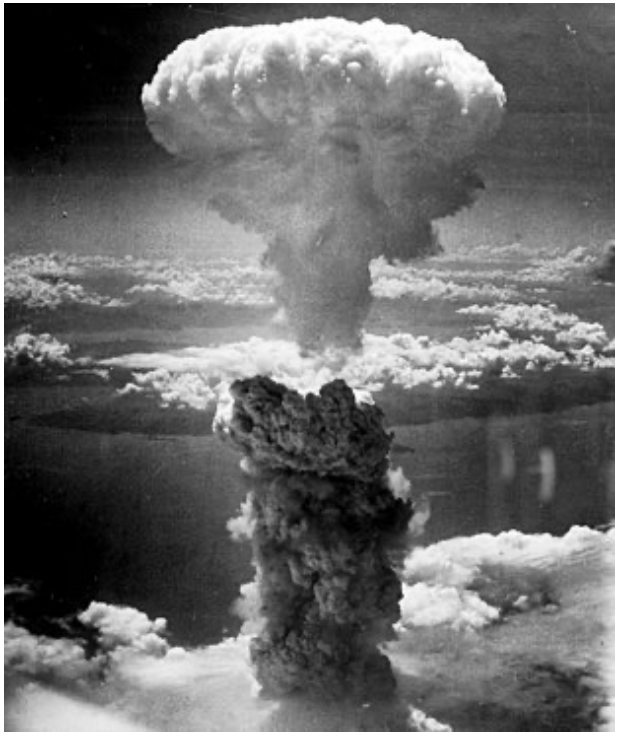
Diphtheria' RT(1922)

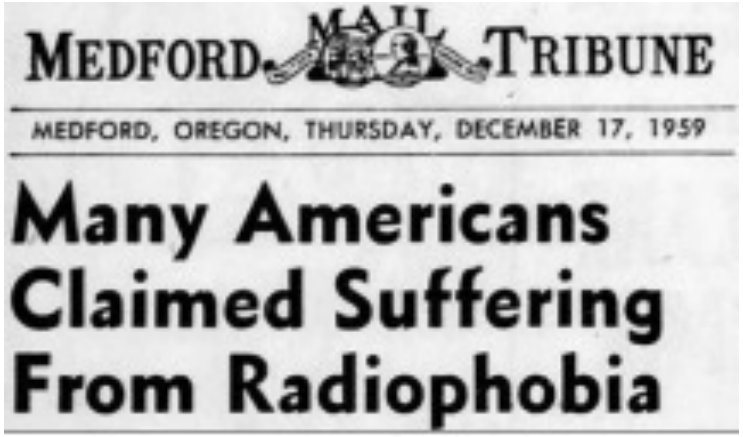
BACKGROUND




THE RADIUM GIRLS
A JAW DROPPING NEW MUSICAL
BOOK BY AMANDA D'ARCHANGELIS, SAMI HORNEFF & LISA MONGILLO
LYRICS BY SAMI HORNEFF & LISA MONGILLO
MUSIC BY AMANDA D'ARCHANGELIS

BACKGROUND




MEDFORD MAIL TRIBUNE

MEDFORD, OREGON, THURSDAY, DECEMBER 17, 1959

Many Americans Claimed Suffering From Radiophobia

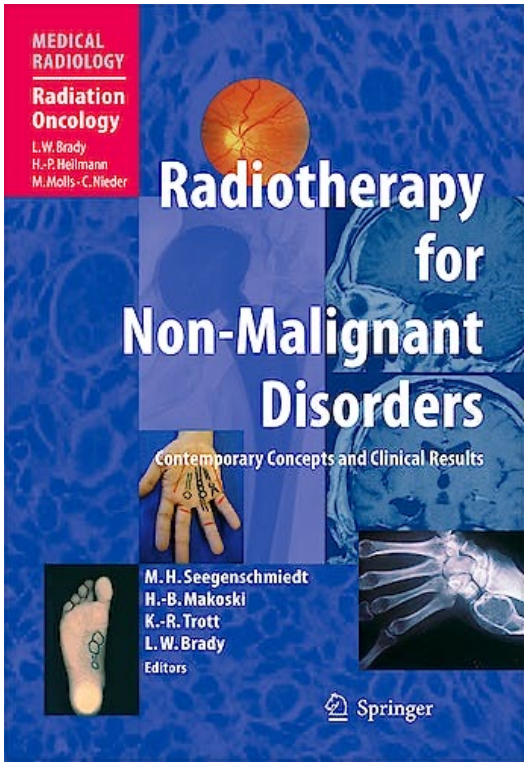
INTRODUCTION

DEGRO
DEUTSCHE GESELLSCH
FÜR RADIOONKOLOGIE

BenigNews
Founded in 2000
Official Letter of the German Cooperative Group on Radiotherapy for Benign Diseases (GCG-BD) and Cooperating Groups

German Cooperative Group
Radiotherapy
for Benign Diseases

Prof. Michael Heinrich Seegenschmiedt



2007

Radiotherapy for non-malignant disorders: state of the art and update of the evidence-based practice guidelines

[1]M H SEEGENSCHMIEDT, MD, PhD, [2]O MICKE, MD, PhD and [3,4]R MUECKE, MD, PhD; the German Cooperative Group on Radiotherapy for Non-malignant Diseases (GCG-BD)

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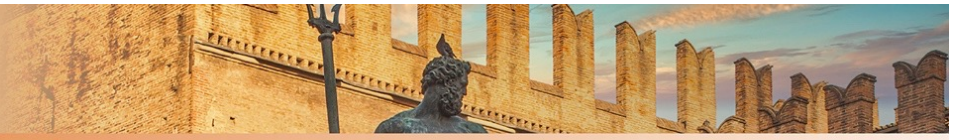
[2]Department of Radiotherapy and Radiation Oncology, Franziskus Hospital Bielefeld, Bielefeld, Germany
[3]Department of Radiotherapy, Lippe Hospital Lemgo, Lemgo, Germany
[4]Department of Radiotherapy and Radiation Oncology, Marien Hospital Herne, Ruhr University Bochum, Bochum, Germany

2015

AIRO2022
XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI
Radioterapia di precisione per un'oncologia innovativa e sostenibile



Journal of *Personalized Medicine*

MDPI

Review

Non-Oncological Radiotherapy: A Review of Modern Approaches

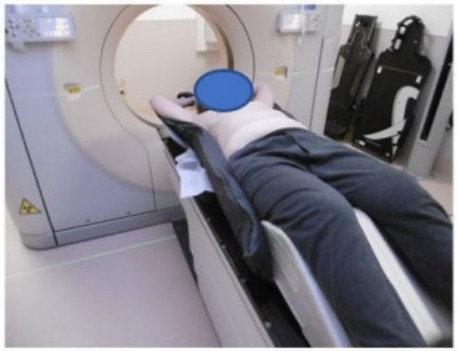
Valerio Nardone [1,*,†], Emma D'Ippolito [1,†], Roberta Grassi [1], Angelo Sangiovanni [1], Federico Gagliardi [1], Giuseppina De Marco [1], Vittorio Salvatore Menditti [1], Luca D'Ambrosio [1], Fabrizio Cioce [1], Luca Boldrini [2], Viola Salvestrini [3], Carlo Greco [4], Isacco Desideri [3], Francesca De Felice [5], Ida D'Onofrio [6], Roberto Grassi [1], Alfonso Reginelli [1,‡] and Salvatore Cappabianca [1,‡]

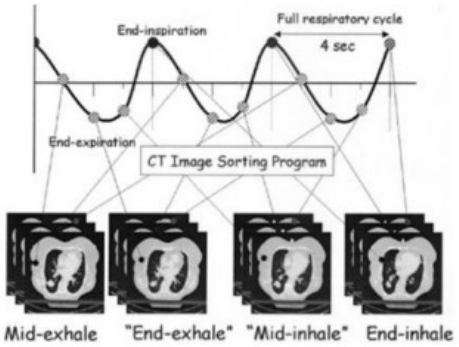
1 Department of Precision Medicine, University of Campania "L. Vanvitelli", 80138 Naples, Italy
2 Radiation Oncology, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Largo Agostino Gemelli, 00168 Rome, Italy
3 Radiation Oncology, Azienda Ospedaliero-Universitaria Careggi, Department of Experimental and Clinical Biomedical Sciences, University of Florence, 50134 Florence, Italy
4 Department of Radiation Oncology, Università Campus Bio-Medico di Roma, Fondazione Policlinico Universitario Campus Bio-Medico, Via Alvaro del Portillo, 00128 Rome, Italy
5 Radiation Oncology, Policlinico Umberto I "Sapienza" University of Rome, Viale Regina Elena 326, 00161 Rome, Italy
6 Radiation Oncology, Ospedale del Mare, ASL Napoli 1 Centro, 80147 Naples, Italy

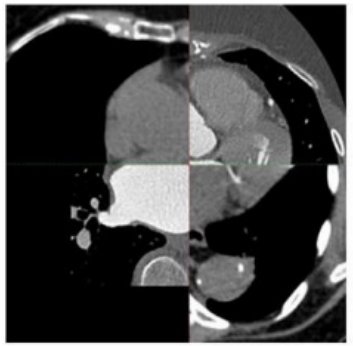
Ventricular Tachycardia
&
Atrial Fibrillation

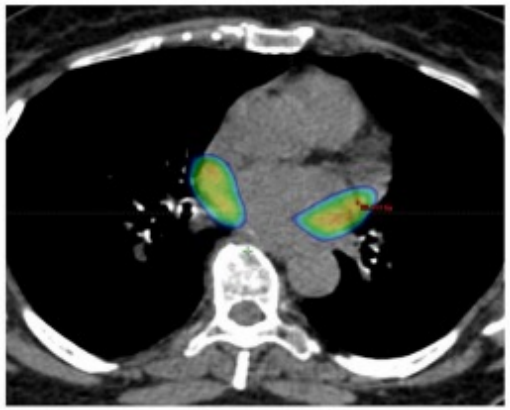
Authors	Year	N pts	Diagnosis	End-Point	Dose tot/fx	Results
Cuculich PS [12]	2017	5	VT	Efficacy and safety of treatment	25 Gy/1 fx	No complications during treatment. Fatigue after treatment (three patients), with no acute heart-failure. Marked reduction in the burden of ventricular tachycardia after treatment.
Kurzelowski R [13]	2022	2	VT	Efficacy and safety of treatment	25 Gy/1 fx	No problem in the first patient. The second one experienced acute side effects with an increase in VT that gradually improved at the end of the follow-up period.
Wight J [14]	2022	14	VT	Efficacy and safety of treatment	25 Gy/1 fx	VT was reduced in 59%, ATP was reduced in 39%, and shocks were reduced in 60%.
Lee J [15]	2021	7	VT	Reduction of VT and safety of treatment	25 Gy/1 fx	VT responded in all patients. After 6 months, VT burden was reduced by 85%. No high grade acute toxicity.
Piccolo C [16]	2022	Phantom study	VT	Feasibility of Cyberknife on cardiac lesions by tracking as a single marker the lead tip of an implantable cardioverter defibrillator.	25 Gy/1 fx	Tracking with a single marker is feasible considering adequate residual planning margins. The volumes could be further reduced by using additional markers.
Bonaparte I [17]	2021	Dosimetric study	VT	STAR is efficacy in terms of BDT and MUs.	25 Gy/1 fx	Several plans were evaluated for dosimetric considerations.
Kovacs B [18]	2021	57	VT/FA	STAR's effectivity and safety for structural VT/VF	25 Gy/1 fx	Significant short-term reduction of sustained VT/VF-burden, but recurrences are common.
Akdag O [19]	2022	Phantom study	VT	First experimental evidence for real-time cardiorespiratory motion-mitigated MRI-guided STAR on the 1.5 T Unity MRlinac aimed at simultaneously compensating cardiac and respiratory motions.	25 Gy/1 fx	Cardiac motion was successfully mitigated using gating, which was demonstrated in the phantom and in-silico experiment.
Kautzner J [20]	2021	3	VT	postmortem immunohistochemical was performed early and late after SBRT	25 Gy/1 fx	Apoptosis and subsequent fibrosis was shown to be not immediate, thus the antiarrhythmic effects may be delayed after SBRT.
Di Monaco A [21]	2022	5	AF	Side effects at 1 month after STAR	25 Gy/1 fx25 Gy/1 fx	No acute treatment-related adverse events (>G1)

Abbreviation: N: number, Pts: patients, RT: radiation therapy, Fx: fractions, VT: Ventricular Tachycardia, AF Atrial Fibrillation, Gy: Gray, STAR: Stereotactic Arrhythmia Radioablation.

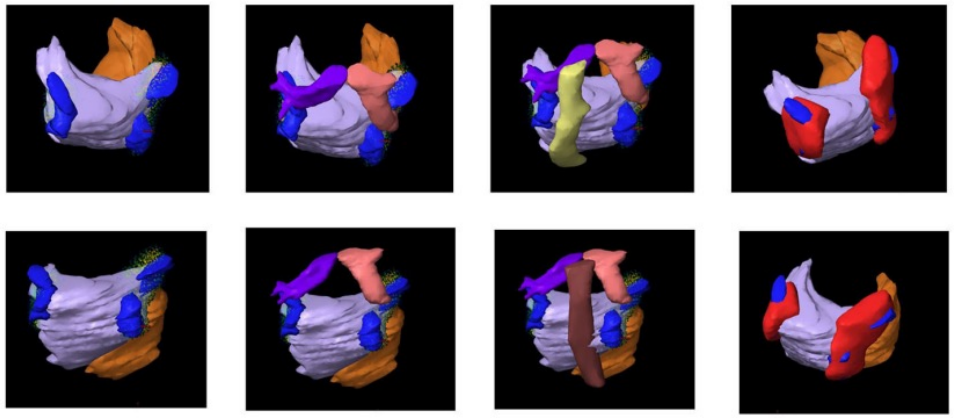




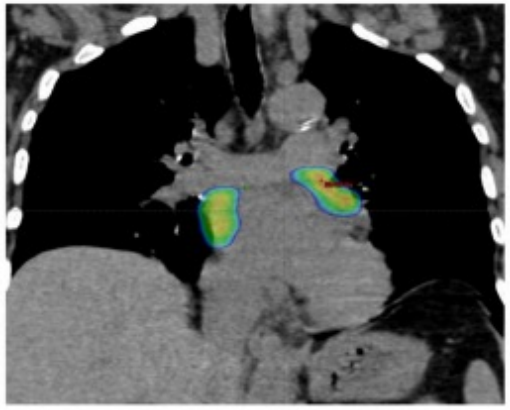




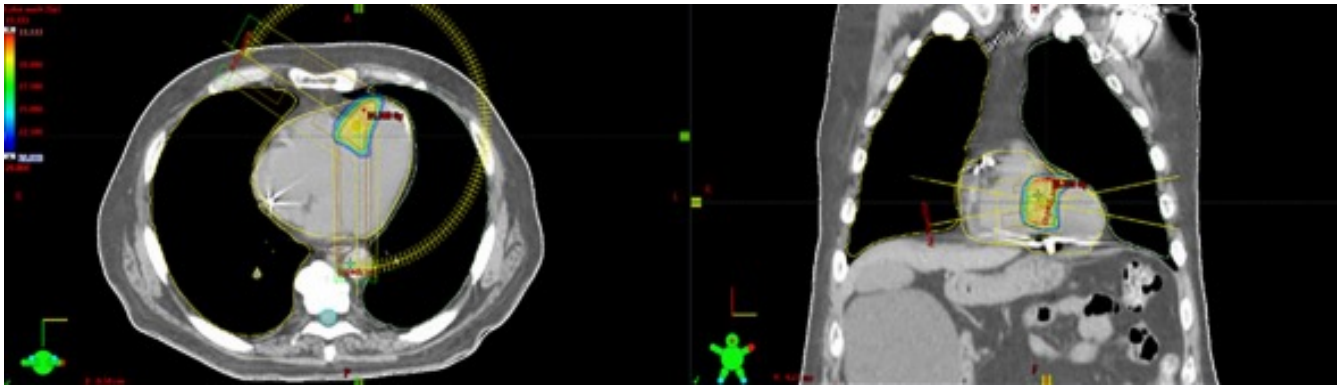
(1) Basic free-breathing CT → (2) 4-Dimension CT → (3) CT with contrast



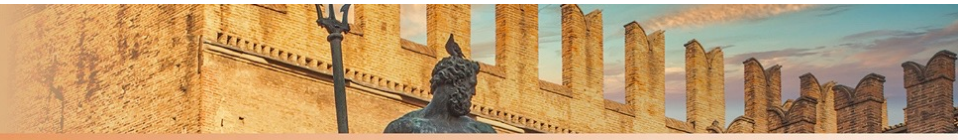
(Blu) Pulmonary Veins; (Purple) Left Atrium; (Orange) Right Atrium; (Violet & Pink) Main Bronchus; (Yellow & Brown) Esophagus [taking into account latero-lateral dislocation]; (Red) Target Volume



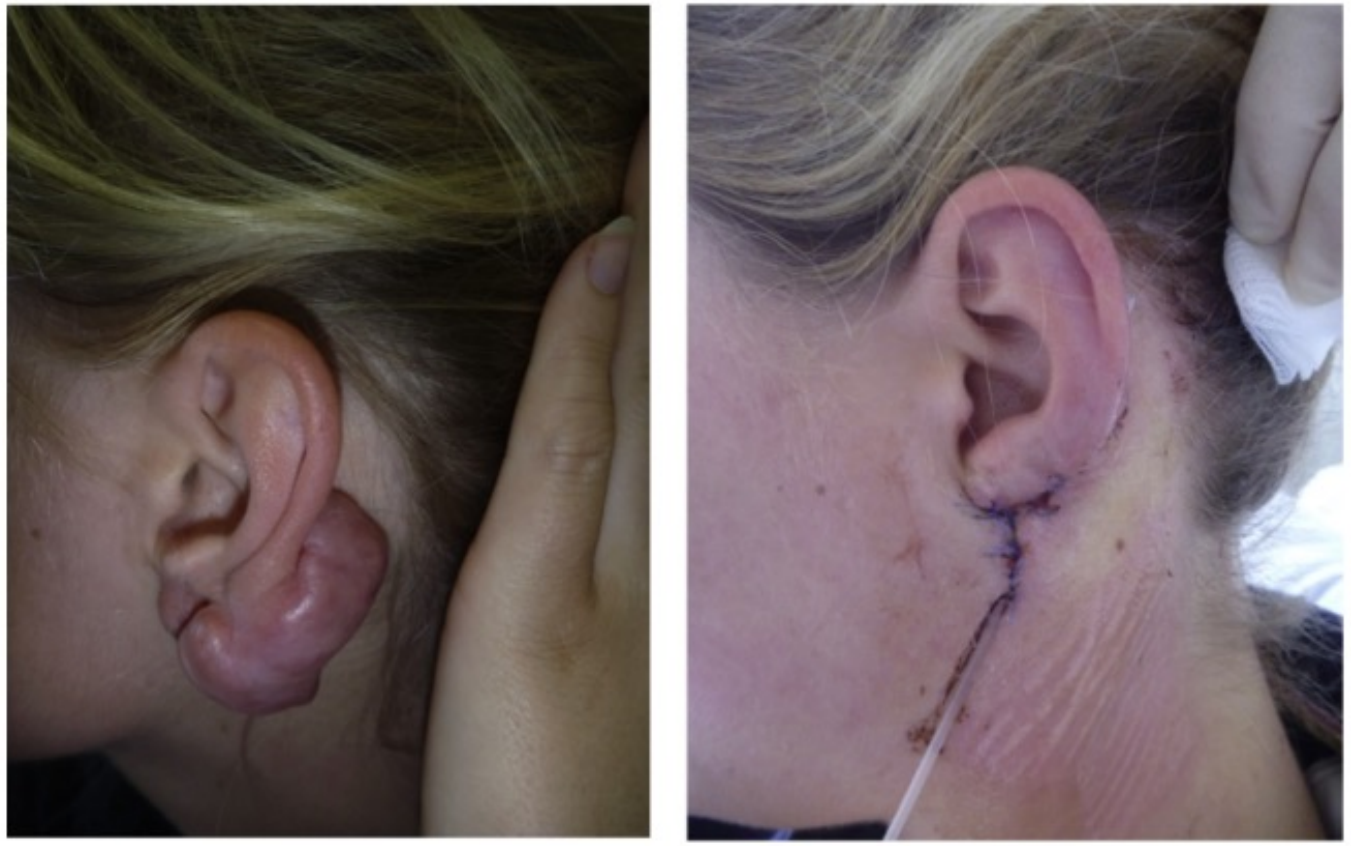
Dose distribution of 25 Gy in 1 fraction for Linac-based stereotactic radiosurgery



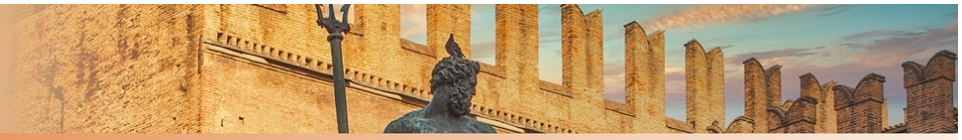
Keloids
Dupuytren's Disease
Peyronie's Disease



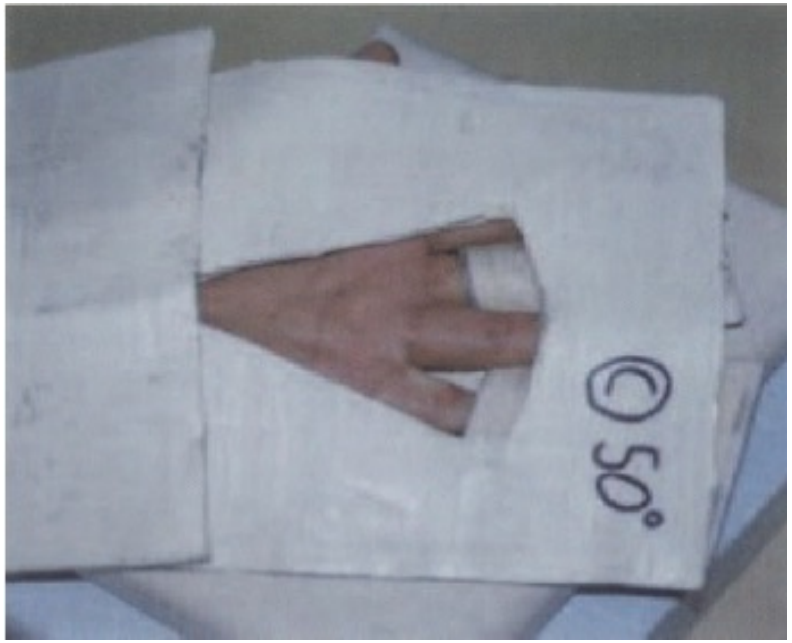
Jiang [29]	2018	29	Keloids	Control rate	18 Gy/3 fx	Response rate 91.9%
Kim [30]	2015	28	Keloids	Control rate	12–15 Gy/3 fx	Response rate 50%
Shen [31]	2015	568	Keloids	Control rate	18 Gy/3 fx	Response rate 90.41%
Emad [32]	2010	26	Keloids	Control rate	12 Gy/3 fx	Response rate 70.4%
Malaker [33]	2004	64	Keloids	Control rate	37.5 Gy/5 fx	Response rate 97%
Lo [34]	1990	199	Keloids	Control rate	2–20 Gy/1 fx	Response rate 87% for Dose > 9 Gy, 43% for Dose < 9 Gy.
Borok [35]	1988	250	Keloids	Control rate	4–16 Gy/various fx	Response rate 98%
Van de Kar [36]	2007	21	Keloids	Control rate	12 Gy/3–4 fx	Response rate 71.9%
Arneja [37]	2008	25	Keloids	Control rate	HDR BT 5 Gy/3 fx	Response rate 92%
Van Leeuwen [38]	2014	67	Keloids	Control rate	HDR BT 6 Gy/2 fx	Response rate 96.9%
Jiang [39]	2016	32	Keloids	Control rate	HDR BT 6 Gy/3 fx	Response rate 94%
Hafkamp [40]	2017	29	Keloids	Control rate	HDR BT 13 Gy/1 fx	Response rate 75.9%

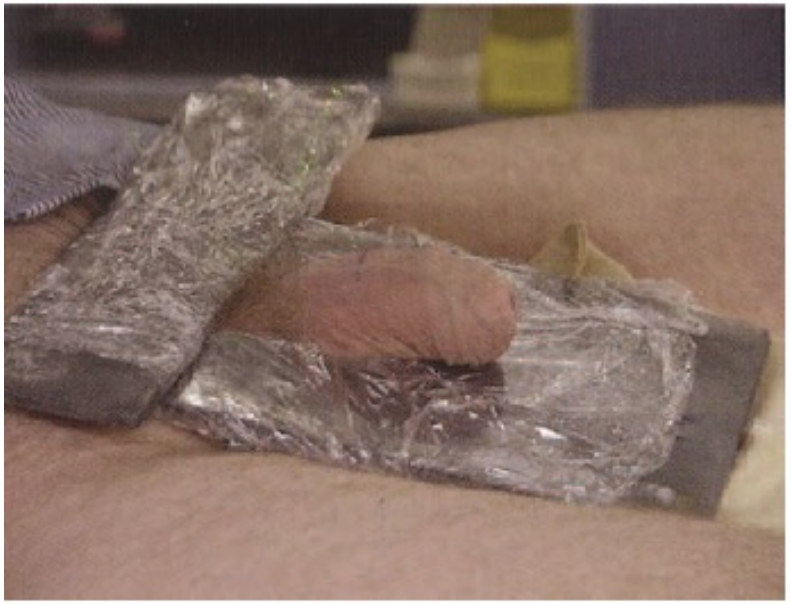


Implantation of a single tube for interstitial brachytherapy after the resection of a retroauricular keloid.

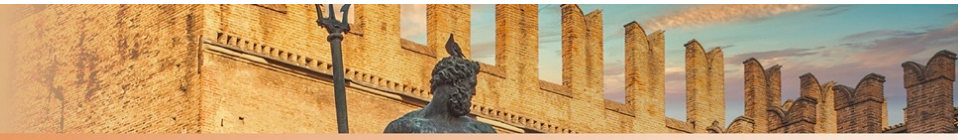


Author	Year	N pts	Diagnosis	End Point	Dose	Results
Seegenschmiedt [7]	2015	1762	Dupuytren's disease	Control rate	15–21 Gy in 5–7 fx, 30 Gy split in 2 series of 5fx with a 3 months interval	Stability of disease in 84% for N stage and 67% for N/I stage
Betz [42]	2010	135	Dupuytren's disease	Control rate	30 Gy split in 2 series of 5 fx separated by a 6- to 8-week interval	Stability of disease in 59%, 10% improved, and 31% progressed. In stage N 87% and in stage N/I 70% remained stable or regressed
Seegenschmiedt [8]	2015	8732	Peyronie's disease	Pain, improvement	10–20 Gy (2–10 fx)	Pain regression in 50–90%, Improvement of penile deviation in 30–70%
Kadhum [41]	2017	698	Dupuytren's disease	Control rate	21–42 Gy in 3–14 fx	Good ratio of regressions (6–20% depending on staging), stability (12–81%) and low ratio of progressions (13–65%, depending on staging).

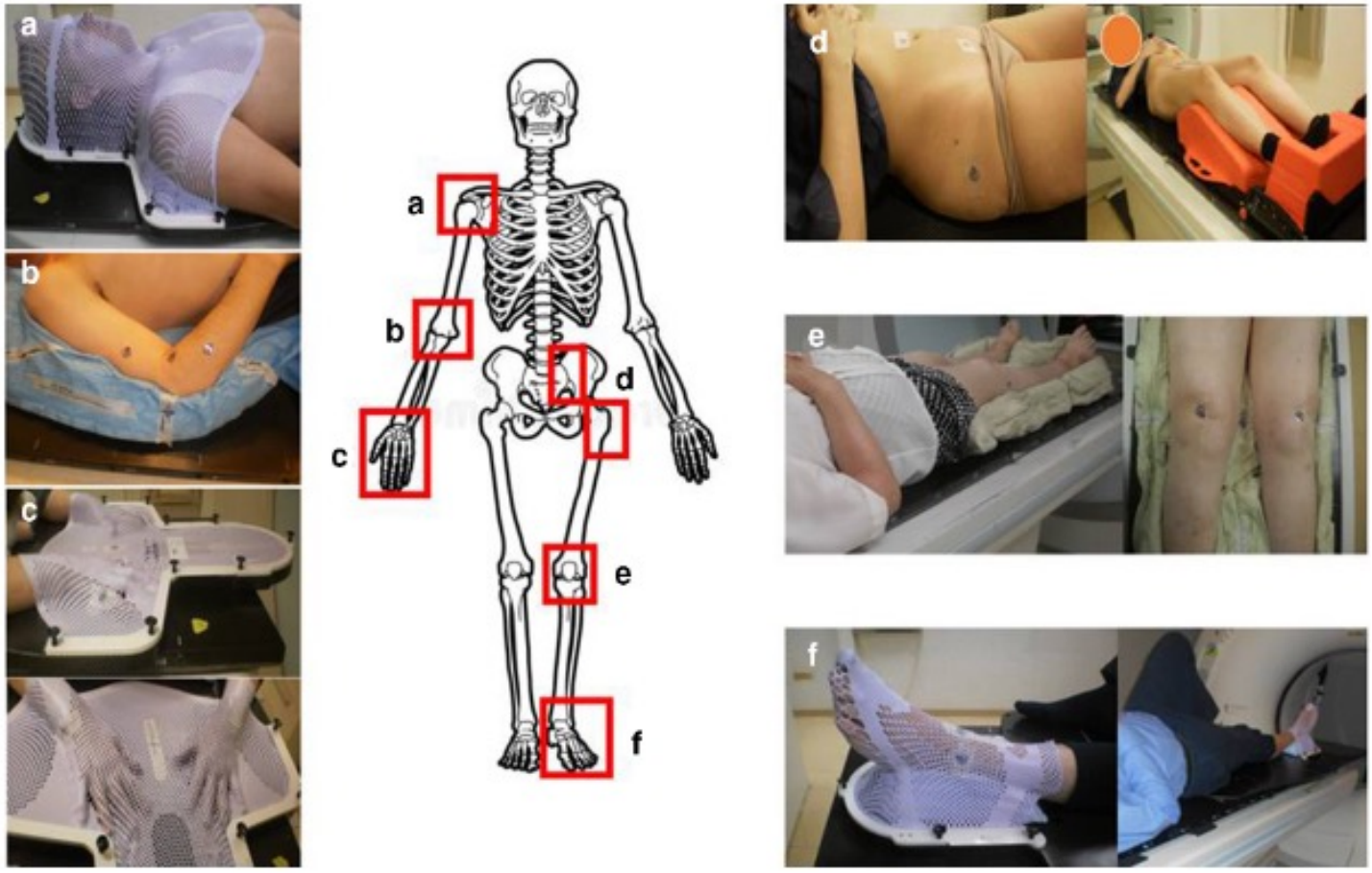




Osteoarthritis
Osteoarthrosis
Achillodynia



Author	Year	N pts	Diagnosis	End Point	Dose	Results
Hautmann [45]	2019	124	epicondylitis humeri	pain relief	6 Gy(1 Gy)–3 Gy (0.5 Gy)	complete response 64% at 24 months
Rogers [46]	2020	157	epicondylitis, plantar fasciitis, and finger osteoarthritis	pain relief	4 Gy (0.5 Gy)–8 Gy Orthovoltage	pain relief at rest and during activity and a corresponding objective improvement in handgrip strength in epicondylitis. Pain relief at rest, during activity and improvement in walking time were demonstrated in plantar fasciitis
Hautmann [47]	2020	86	Humeral epicondylitis	pain relief	3 Gy /2.5 Gy (0.5 Gy /fx); 6 Gy (1 Gy/fx)	
Micke [48]	2018	703	Calcaneodynia, Achillodynia, Bursitis trochanterica, Shoulder Syndrome, Gonarthrosis	pain relief	6 Gy (0.5–1 Gy)	At follow up, good response: Calcaneodynia 80.7%, Achillodynia 88.9%, Bursitis trochanterica 46.3%, Shoulder Syndrome 60%; only Gonarthrosis 29.2%
Alvarez [49]	2019	108	OADD	pain relief	6 Gy (1 Gy)–12 Gy	Overall, and with a follow-up of 8 months (range 1–31 months), 91% of patients experienced pain relief. The pain reported according to the VAS scale was 0–3 in 32.6% of the patients, 4–6 in 36.7% and greater or equal to 7 in 20.1% of treated patients.
Mahler [50]	2018	55	knee osteoarthritis	pain relief	6 Gy	At 3 months follow-up: no substantial beneficial effect on symptoms and inflammatory signs of LDRT in patients knee OA, compared with sham treatment
Ott [51]	2015	112	Achillodynia	pain relief	6 Gy /3 Gy	Pain control:Early 84% Middle-term 88% Long-term 95%
Rudat [52]	2021	666	Heel Spur	pain relief	3 Gy (Re-irradiation possible)	Good local control (>75%) and good response to reirradiation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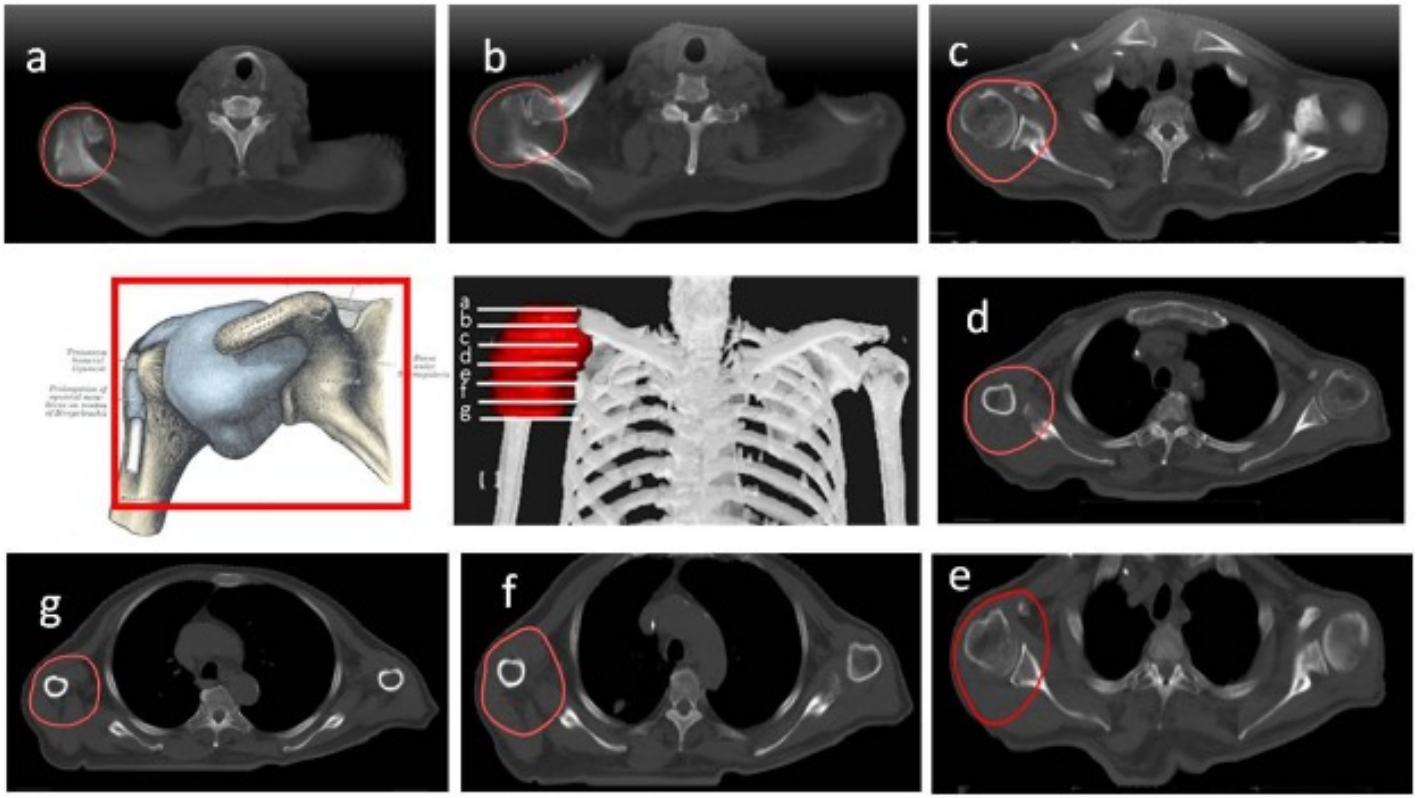
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Epilepsy

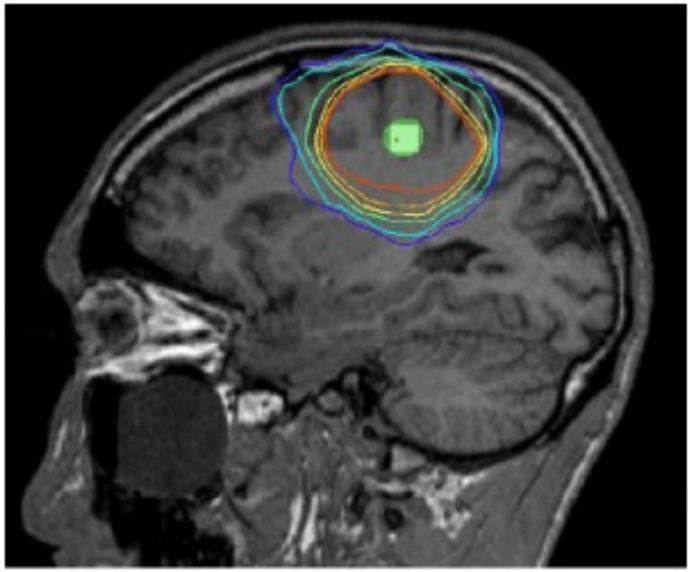
Trigeminal Neuralgia

Brain Arteriovenous Malformations

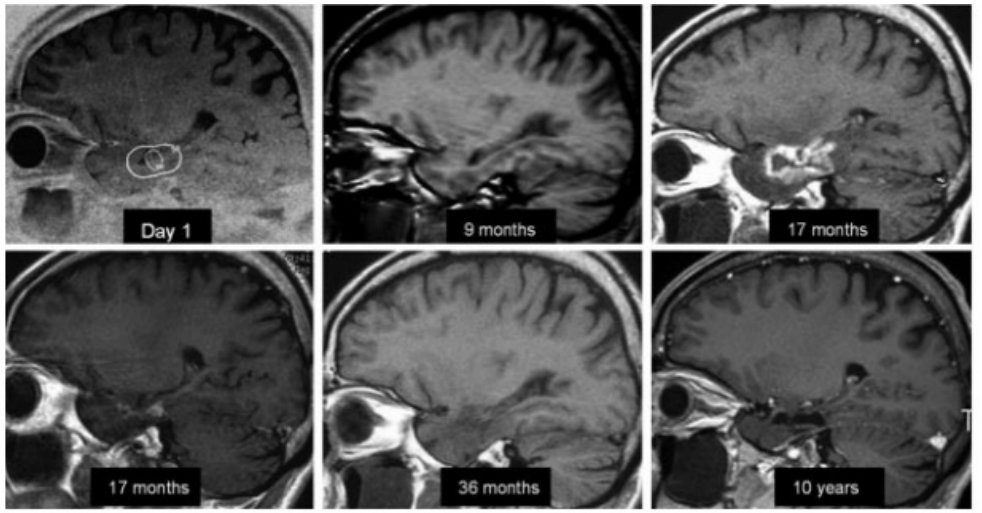
Graves Ophthalmopathy

Epilepsy

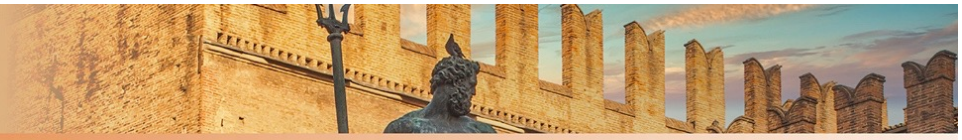
Authors	Year	N pts	Diagnosis	End Point	Dose	Results
Rauch [60]	2012	11	Epilepsy	Tolerability and seizure frequency.	26.3–58.3 Gy	Treatment led to an improvement in the frequency of seizures in 63%.
Liang [61]	2010	7	Epilepsy	Seizure frequency	12 Gy	Reduction of seizure frequency was 50% in two cases, 30% in one case, and 0% in two cases, and seizure frequency increased more than 100% in two cases.
Bartolomei [62]	2008	15	Epilepsy	Seizure frequency	24 Gy	A total of 60% pts were considered seizure free. All patients who were initially seizure free experienced a relapse of isolated aura (66%) or complex partial seizures (66%) during antiepileptic drug tapering.
Barbaro [63]	2009	28	Epilepsy	Seizure frequency	24 Gy high dose vs. 20 Gy low dose	At the 36-month follow-up evaluation, 67% of patients were free of seizures for the prior 12 months (high dose: 10/13, 76.9%; low dose 10/17, 58.8%)



Epilepsy



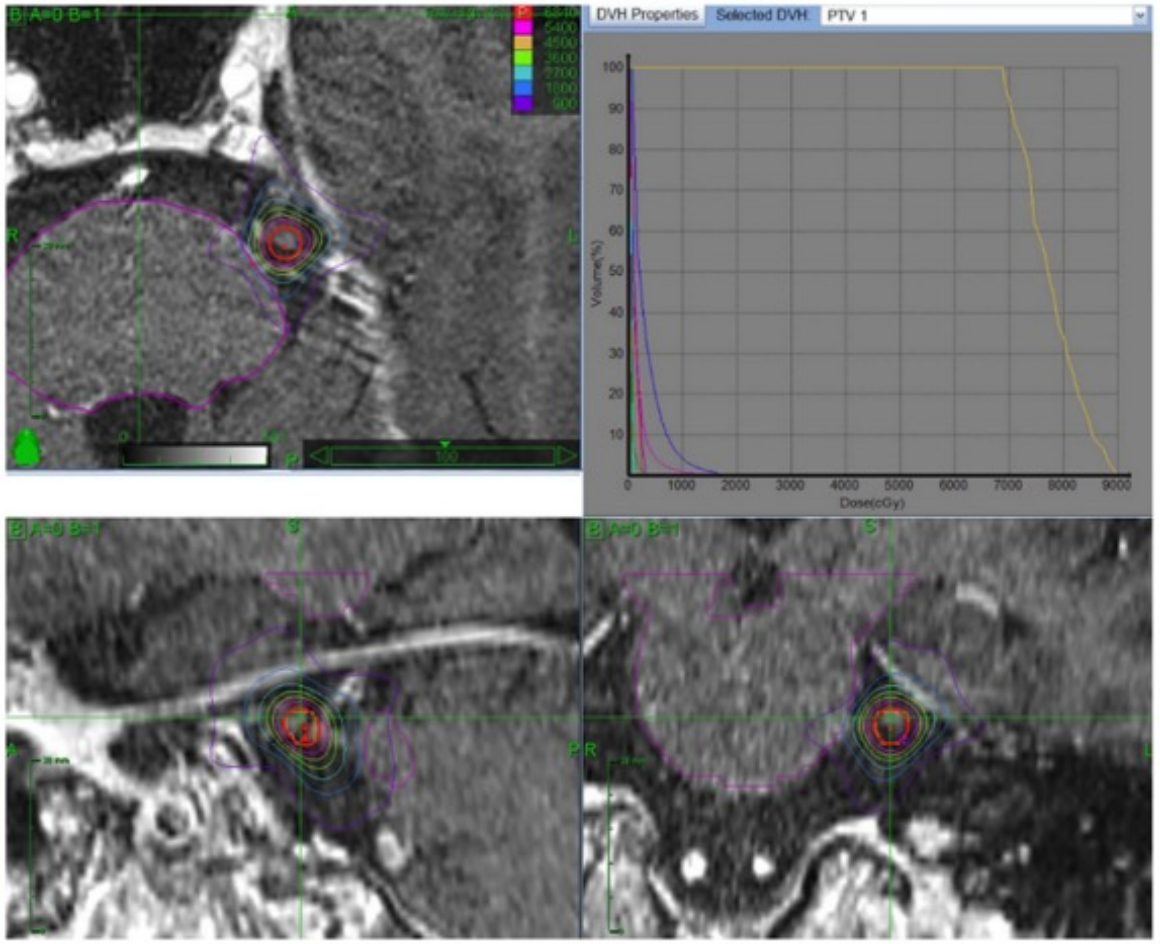
In this case, prominent changes are seen at 17 months: inside the target volume is a heterogeneous T1 signal hypointensity and a contrast enhancement ring corresponding to the periphery of the target region. A gradual disappearance of signs over time was observed. Last MRI shows a residual necrotic cavity in the target volume.

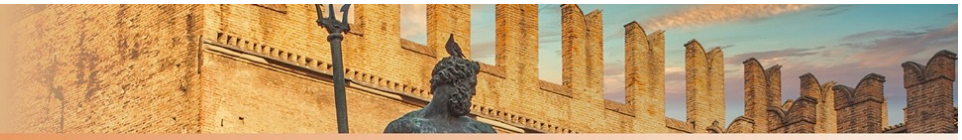


Trigeminal Neuralgia

Authors	Year	N pts	Diagnosis	End Point	Dose	Results
Smith [64]	2011	169	TN	Pain relief	70–85 Gy, 90 Gy	A total of 79.3% experienced significant relief. A total of 19.0% had recurrent pain. Of 87 patients with idiopathic TN without prior procedures, 79 (90.8%) had initial relief. Among 28 patients treated with 70 Gy, 18 patients (64.3%) had significant relief. Of the patients with 90 Gy at the brainstem, 59 (79.0%) had significant relief.
Rashid [65]	2018	55	TN	Pain relief	90 Gy	After 30 months median follow-up, 69% of patients were pain free.
Romanelli [66]	2019	387	TN	Pain relief	60 Gy (80% isodose)	Pain relief rate at 6, 12, 18, 24, 30, and 36 months was, respectively, 92, 87, 87, 82, 78, and 76%.
Lovo [67]	2019	14	TN	Pain relief	140 Gy	A total of 90% pts reported some form of relief. A total of 60% reached the threshold of 50% pain relief, and for 40% the pain never improved.
Kundu [68]	2022	41	TN	Pain relief	90 Gy	There has been a significant improvement in the post-radiation pain score in 72% of patients.

Trigeminal Neuralgia

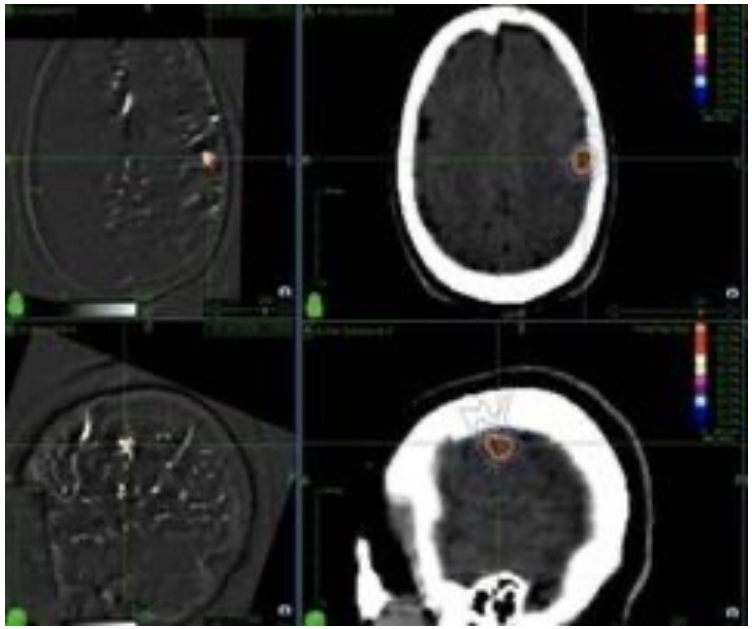




Authors	Year	N pts	Diagnosis	End Point	Dose	Results
Starke [69]	2016	2236	AVM	Obliteration rate	20.5 Gy (mean margin dose)	Overall obliteration rate was 64.7%.
Ding [70]	2017	232	AVM	Obliteration rates, hemorrhage rate	22.5 Gy	The actuarial obliteration rates at 5 and 10 years were 72% and 87%, respectively. Annual post-SRS hemorrhage rate was 1.0%
Patibandla [71]	2017	233	AVM	Obliteration rates, hemorrhage rate in Grade III-IV AVMs	Mean dose 17.3 Gy	The actuarial obliteration rates at 3, 7, 10, and 12 years were 15%, 34%, 37%, and 42%, respectively. The annual post-SRS hemorrhage rate was 3.0%
Matsuo [72]	2014	51	AVM	Obliteration rate	15 Gy (80% isodose)	The actuarial obliteration rates at 3, 5, 10, and 15 years were 46.9%, 54.0%, 64.4%, and 68.0%, respectively

Brain Arteriovenous Malformations

Brain Arteriovenous Malformations



Graves Ophthalmopathy

Authors	Year	N pts	Diagnosis	End Point	Dose	Results
Matthiesen [73]	2012	211	GO	Symptomatic improvement	20 Gy/10 fx	A total of 84.2% pts reported a symptomatic improvement
Kouloulias [74]	2013	17	GO	Symptomatic improvementand tolerability	20 Gy/10 fx	Stabilization of the disease without recurrence was achieved in 12/17 patients. At the end of radiotherapy, the CAS regressed to 4.82 ± 2.24 ($p < 0.001$, Wilcoxon test). Extraocular motility and pain behind the globe were improved in 14/17 and 16/17 patients, respectively. Five patients developed recurrent signs and symptoms and they underwent surgical decompression
Li Yim [75]	2011	59	GO	duration of symptoms, clinical activity score (CAS)	20 Gy/12 fx (over 2 weeks)	Response (change in CAS) to orbital radiotherapy was statistically significant from 3.17 ± 1.75 standard deviation (SD) to 0.73 ± 0.92 SD ($p < 0.001$)
Kahaly [76]	2000	65	GO	Symptomatic improvement and toxicity	A: 20 Gy/20 fx (over 20 weeks) B: 10 Gy/10 fx (over 2 weeks) C: 20 Gy/10 fx (over 2 weeks)	Response to therapy, defined as a significant amelioration of three objective parameters, was noted in 12 A (67%), 13 B (59%), and 12 C (55%) subjects (C vs. A, $p = 0.007$). Ophthalmic symptoms and signs regressed most in group A
Cardoso [77]	2012	18	GO	Symptomatic improvement and Radiologic response	10 Gy/10 fx (over 10 weeks)	Significant decrease in symptoms such as tearing ($p < 0.001$), diplopia ($p = 0.008$), and conjunctival hyperemia ($p = 0.002$). Magnetic resonance imaging showed decrease in ocular muscle thickness and in the intensity of the T2 sequence signal in the majority of patients

Graves Ophthalmopathy

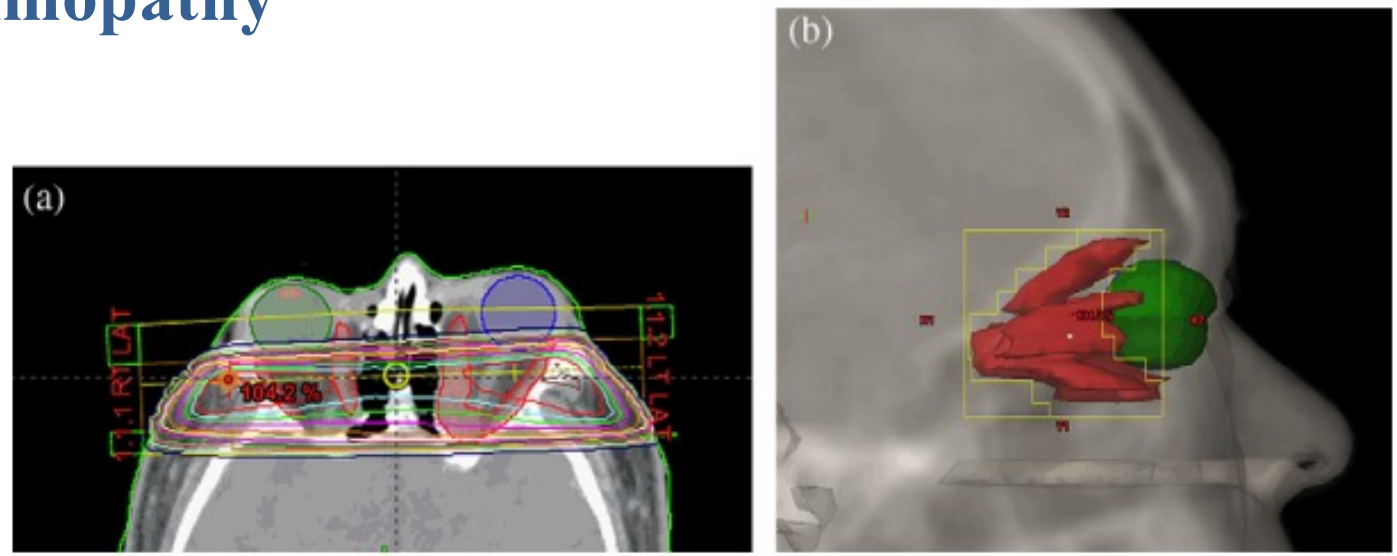
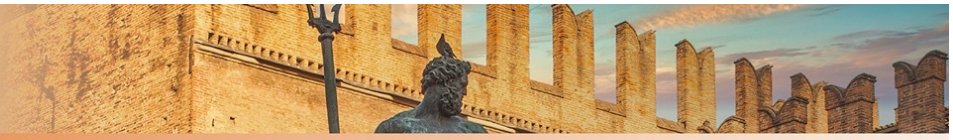
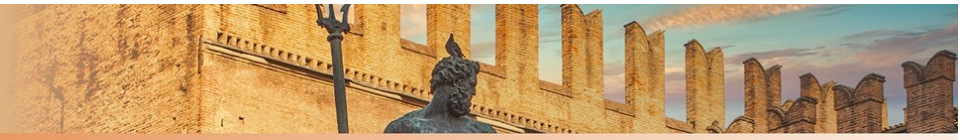


Fig. 2. (A) Typical isodose plan for Graves' orbitopathy. (B) Beam's-eye view of lateral photon field.

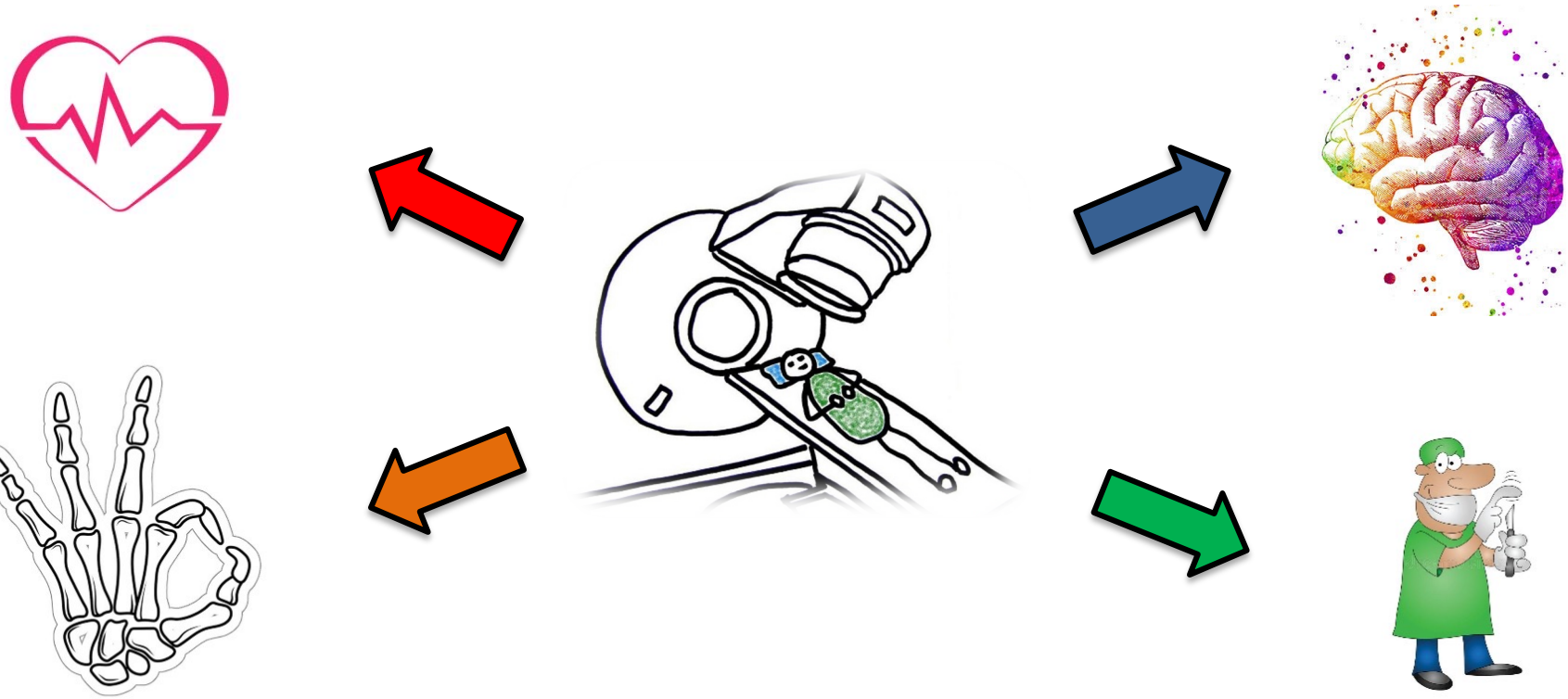


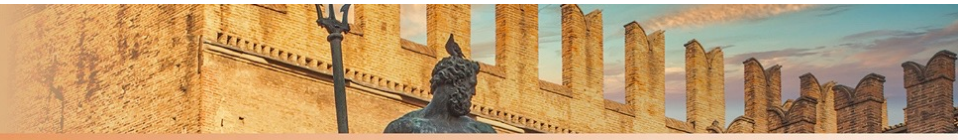
NCT Number	Disease	Design	Location
NCT04722263	Keloids	Single arm, interventional pilot study (15 patients). RT: 15 Gy in 3 fractions.	Montefiore Medical Center, New York, US
NCT04122313	Dupuytren's Disease	Prospective, Cohort study. Participants will be treated according to a standard treatment pathway, followed by post-operative radiation. RT: 15 Gy in 5 fx, followed by a 6-8 weeks break then a second identical course. Total dose: 30Gy.	University of Minnesota, US
NCT04424628	Gonarthrosis and Coxarthrosis	Non-inferiority study in which the investigators compare two low-dose radiotherapy schemes. Arm A will be treated at 3 Gy (0.5 Gy/fraction, 3 fractions/week), and patients in arm B will be treated at 6 Gy (1 Gy/fraction, 3 fractions/week).	GenesisCare, Malaga, Spain
NCT02708810	Trigeminal Neuralgia	To determine the feasibility of frameless Virtual Cone trigeminal neuralgia radiosurgery at a single institution prior to multi-institutional enrollment.	Hazelrig-Salter Radiation Oncology Center, Birmingham, Alabama, US
NCT03995823	Cerebral Arteriovenous Malformations	Prospective study including 50 patients with cerebral AVMs treated with GRKS to evaluate the sensitivity for nidus obliteration of MRI.	Department of Neurosurgery, Medical University of Vienna, Austria
NCT04843683	Cardiac Arrhythmias	Prospective, single-center, phase II trial that will be monitoring the safety and efficacy of using stereotactic ablative radiotherapy (SBRT) to treat arrhythmias.	University Health Network, Toronto, Canada



CONCLUSIONS

- The NORT can be considered safe and effective for the not malignant disease,
- Modern dosimetry,
- Use of the NORT for elderly patients ineligible for invasive treatment.





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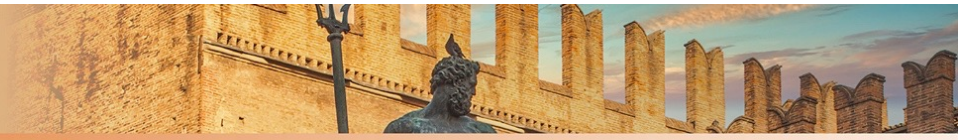

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BACK TO THE NORT

Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

GRAZIE PER L' ATTENZIONE