Radiation Therapy for Nonmalignant Diseases in Germany

Current Concepts and Future Perspectives

M. Heinrich Seegenschmiedt[1, 2], Oliver Micke[2], Norman Willich[2], and the German Cooperative Group on Benign Diseases (GCG-BD)

Background: Radiotherapy (RT) of nonmalignant diseases has a long-standing tradition in Germany. Over the past decade significant theoretical and clinical progress has been made in this field to be internationally recognized as an important segment of clinical RT. This development is reflected in a national patterns-of-care study (PCS) conducted during the years 2001–2002.
Material and Methods: In 2001 and 2002, a questionnaire was mailed to all RT facilities in Germany to assess equipment, patient accrual, RT indications, and treatment concepts. 146 of 180 institutions (81%) returned all requested data: 23 university hospitals (UNI), 95 community hospitals (COM), and 28 private institutions (PRIV). The specific diseases treated at each institution and the RT concepts were analyzed for frequencies and ratios between the different institution types. All data were compared to the first PCS in 1994–1996.
Results: In 137 institutions (94%) 415 megavoltage units (mean 1.7; range 1–4), and in 78 institutions (53%) 112 orthovoltage units (mean 1.1; range 0–2) were available. A mean of 37,410 patients were treated per year in all institutions: 503 (1.3%) for inflammatory disorders, 23,752 (63.5%) for degenerative, 1,252 (3.3%) for hypertrophic, and 11,051 (29.5%) for functional, other and unspecified disorders. In comparison to the first PCS there was a significant increase of patients per year (from 20,082 to 37,410; +86.3%) in most nonmalignant diseases during the past 7–8 years. Most disorders were treated in accordance with the national consensus guidelines: the prescribed dose concepts (single and total doses) varied much less during the period 2001–2002 in comparison with the previous PCS in 1994–1996. Only five institutions (3.4%) received recommendations to change single or total doses and/or treatment delivery. Univariate analysis detected significant institutional differences in the use of RT for various disorders.
Conclusion: RT is increasingly accepted in Germany as a reasonable treatment option for many nonmalignant diseases. The long-term perspective and research plan will have to include various updates of PCS, rewriting of consensus guidelines, introduction of registries for rare nonmalignant disorders, and clinical controlled studies even for so-called established indications, as international acceptance is based on the criteria of evidence-based medicine.

KeyWords: Radiotherapy of nonmalignant diseases · Patterns-of-care study · Quality assurance · Inflammatory/degenerative/hyperproliferative/functional disorders

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Radiotherapie nichtmaligner Erkrankungen in Deutschland. Aktuelle Konzepte und Perspektiven

Hintergrund: Die Radiotherapie (RT) nichtmaligner Erkrankungen hat eine lange Tradition in Deutschland. Im letzten Jahrzehnt wurden theoretische und klinische Fortschritte gemacht, die diesem Bereich der RT auch international eine erhebliche Bedeutung verschafft haben. Die positive Entwicklung stützt die jüngste Patterns-of-Care-Studie (PCS) der Jahre 2001–2002.
Material und Methodik: Im Jahr 2001 und 2002 wurden anhand eines Fragebogens an allen deutschen strahlentherapeutischen Institutionen die technische Ausstattung, Patientenzuweisung, Indikationen und RT-Konzepte bei nichtmalignen Erkrankungen erfasst. 146 von 180 Institutionen (81%) machten vollständige Angaben: 23 Universitätskliniken (UNI), 95 Versorgungskrankenhäuser (COM) und 28 private Praxen (PRIV). Die einzelnen Krankheitsgruppen und Erkrankungen pro Institution und die RT-Konzepte wurden nach Häufigkeit und Verhältnis zwischen den Institutionen analysiert und mit der ersten PCS aus den Jahren 1994–1996 verglichen.

[1] Department of Radiation Oncology and Radiation Therapy, Alfried Krupp Hospital, Essen, Germany,
[2] Department of Radiation Oncology and Radiation Therapy, Westphalian Wilhelms University Münster, Münster, Germany.

This paper is dedicated to Professor Rolf Sauer, MD, chair of the Department of Radiation Oncology, University of Erlangen, on the occasion of his 65th birthday.

Ergebnisse: In 137 Institutionen (94%) standen 415 Megavolt-Geräte (Mittel 1,7; Spanne 1–4) und in 78 Institutionen (53%) 112 Orthovolt-Geräte (Mittel 1,1; Spanne 0–2) zur Verfügung. Im Mittel wurden insgesamt 37 410 Patienten pro Jahr behandelt: 503 (1,3%) wegen entzündlicher, 23 752 (63,5%) wegen degenerativer, 1 252 (3,3%) wegen hyperproliferativer und 11 051 (29,5%) wegen funktioneller, anderer und nicht spezifizierter Erkrankungen. Im Vergleich zur ersten PCS vor 7–8 Jahren stieg die Patientenzahl pro Jahr signifikant an (von 20 082 auf 37 410; +86,3%). Die meisten Erkrankungen wurden gemäß den nationalen Konsensus-Leitlinien behandelt: Die Dosierungskonzepte (Einzel- und Gesamtdosis) schwankten im Zeitabschnitt 2001–2002 weit weniger als bei der vorherigen PCS von 1994–1996. Nur fünf Institutionen (3,4%) wurde aufgrund der eingereichten Daten eine Änderung der Einzel- und Gesamtdosis oder der Bestrahlungstechnik empfohlen. Es fanden sich univariat statistisch signifikante Unterschiede zwischen den einzelnen Institutionen und Krankheitsgruppen.

Schlussfolgerung: Die RT wird in Deutschland zunehmend als Behandlungsoption für viele nichtmaligne Erkrankungen akzeptiert. Die langfristige Perspektive und Forschung auf diesem Gebiet müssen neben der Aktualisierung von PCS auch die Überarbeitung der Konsensus-Leitlinien, die Einführung von Registern für seltene Erkrankungen und die Durchführung kontrollierter Studien auch bei „etablierten Indikationen" zum Ziel haben, da die internationale Akzeptanz allein auf den Kriterien der evidenzbasierten Medizin aufbaut.

Schlüsselwörter: Radiotherapie nichtmaligner Erkrankungen · Patterns-of-Care-Studie · Qualitätssicherung · Entzündliche/degenerative/hyperproliferative/funktionelle Erkrankungen

Introduction

The use of radiotherapy (RT) for nonmalignant disorders has a long tradition in Germany, but according to an international survey the clinical acceptance varies worldwide [14]; a low acceptance rate and level of professional practice have been observed in Anglo-American countries [21], as old fears for tumor induction are still not resolved . Moreover, legal restrictions (threat of malpractice), organizational and institutional reasons (availability of RT equipment only in cancer centers), and competing treatment options prevent a broader acceptance. Basic research on ionizing radiation for nonmalignant diseases is developing slowly. Only a few prospective clinical studies have been systematically conducted to define dose-response curves and compare RT with other therapies [2, 36]. A first general patterns-of-care study (PCS) was conducted during the period of 1994–1996 to assess the clinical potential of these indications in Germany [28].

Since 1996 the German Society for Radiation Oncology (DEGRO) and the German Cooperative Group on Benign Diseases (GCG-BD) coordinate the scientific, clinical and practical exchange of knowledge and experience in the field of nonmalignant diseases. Major goals of the group are the development and improvement of quality assurance (QA) measures and consensus guidelines for RT of nonmalignant diseases [16], the coordination of controlled clinical trials and implementation of RT as accepted therapeutic option in medical specialties such as general medicine, internal medicine, surgery, orthopedics, etc. Starting out from a first and general PCS in all German RT facilities [28], other national PCS have been conducted on specific disease entities such as heterotopic ossification prophylaxis [20, 33], keloids [13], Graves' orbitopathy [7], plantar fasciitis [19], and desmoids or aggressive fibromatosis [17]. Other specific national PCS and registries for rare nonmalignant disorders are planned (Table 1).

Nevertheless, progress and changes are best assessed, if the first general PCS between 1994–1996 [16] is compared with an update of the quality of RT equipment, range of clinical indications, number of patients treated per institution, and specific RT prescriptions for each nonmalignant disease in various German RT institutions. This was the major rationale to conduct a second general PCS about 7–8 years later. This paper summarizes the results of this update between 2001–2002 including 146 of 180 institutions (81%) in Germany. A perspective is provided on further steps and initiatives to advance the field in the near future.

Material and Methods

A questionnaire (see Appendix) was mailed to all German RT departments in 2001 and 2002 in order to identify their specific institutional experience with RT for nonmalignant diseases. Similar to our first published questionnaire and a European questionnaire [14] single disease entities and four "traditional disease categories" were assessed: inflammatory, degenerative, hyperproliferative, and functional disorders. Data from institutions, which did only provide the numbers for the single disease categories, but not for the specific diseases themselves, were grouped as "not specified" within the respective diseases. For clarification additional statements were requested for each disease entity or category leaving some results without comparison to the former PCS.

The mean annual values for each disease were calculated from the consecutive numbers of patients provided by the different institutions between the years 2001–2002. Data on the technical equipment of each institution were directly obtained from the individual institution despite older figures having been published and used for the PCS in 1994–1996. Similar to the first PCS, the patient accrual per each institution, the key diagnoses and the RT prescriptions were analyzed. The simi-

Table 1. National patterns-of-care studies (PCS) for nonmalignant diseases. Past and future projects.
Tabelle 1. Patterns-of-Care-Studien für nichtmaligne Erkrankungen. Bisherige und zukünftige Projekte.

Year	Nonmalignant disease	Status	Publications [References]
1994–1996	General German PCS for nonmalignant diseases	Finished	Strahlenther Onkol 1999;175:541–7 [28]
1997–1999	German consensus guidelines for nonmalignant diseases	Finished	Int J Radiat Oncol Biol Phys 2002;52:496–513 [16]
1997–1999	Heterotopic ossification (hip)	Finished	Int J Radiat Oncol Biol Phys 2001;51:756–65 [33]
1997–1999	Heterotopic ossification (other anatomic sites)	Finished	Int J Radiat Oncol Biol Phys 2000;48:241.abstract [20]
1998–2000	Keloids	Finished	Strahlenther Onkol 2003;179:54–8 [13]
1998–2000	Graves' orbitopathy	Finished	Strahlenther Onkol 2003;179:372–6 [7]
2001	Calcaneodynia (plantar fasciitis)	Finished	Int J Radiat Oncol Biol Phys 2004;58:828–43 [19]
2002	Desmoids (aggressive fibromatosis)	Finished	Int J Radiat Oncol Biol Phys 2003;57:Suppl:S252.abstract [17]
2001–2002	General German PCS for nonmalignant diseases	Finished	Results presented in this paper
2004	Langerhans cell histiocytosis (histiocytosis X)	In preparation	
2004	Vertebral hemangioma	In preparation	
	Periarthropathia humeroscapularis	In preparation	
	Epicondylopathia humeroradialis	In preparation	
	Gonarthrosis	In preparation	

larly high response rate (146; 81%) as compared to 1994–1996 (134; 88%) allowed an extensive, representative and comparative data analysis. As in the first PCS and based on the different medical traditions in the eastern and western federal states of Germany, specific regional and hospital type-related differences were also examined.

The statistical description of all relevant parameters included median, mean, standard deviation, and range for all continuous variables, and absolute and relative values for all categorical variables. The differences between the frequencies of groups were analyzed with Fisher's exact and χ^2-test, while the mean values of group frequencies were analyzed with the Student t-test.

Results

Institutional Representation

Out of 180 requested institutional surveys a total of 146 questionnaires were completely returned and contained relevant information on the institutional practice for RT of nonmalignant diseases; 18 RT institutions, which responded, but reported no clinical experience, were excluded from the database; six RT institutions did not respond. Thus, 81% of all German RT institutions are represented in this updated PCS which compares to 134 of 152 RT institutions (88%) which responded to the first survey in 1994–1996. According to the institutional type, 23 university hospital (UNI; 16%) and 95 community hospital (COM) departments (65%) and 28 private RT centers (PRIV; 19%) were represented in this survey, which compares to formerly 30 UNI (33%) and 104 COM departments (68%) and no private centers in 1994–1996.

Technical Equipment

Among all 146 responding RT institutions, 78 (53.4%) had access to a total of 112 orthovoltage units (mean 1.1 ± 0.3; range 1–2 units) per institution. These units had an average age of 29 ± 12 (range 3–41) years, which is much older than the average age of orthovoltage units in the PCS 1994–1996 (mean age: 20 ± 14 years). In comparison to the former PCS of 1994–1996 the number of RT institutions equipped with orthovoltage units (102 of 134; 76%) and the overall number of available orthovoltage units (164; –52) were significantly reduced ($p < 0.05$). By contrast, all responding RT institutions together used a total of 415 megavoltage units (360 linac accelerators; 55 cobalt units) with a mean of 1.7 ± 0.8 (range 1–4) megavoltage units per institution. This compares to only 282 megavoltage units (178 linear accelerators; 104 cobalt units) in 1994 –1996. These linear accelerators had an average age of 7.2 ± 3.6 (range 1–18) years. There was no difference with regard to the technical equipment and the institutional type.

Overall Diagnostic Spectrum

During the period 2001–2002 an average of 37,410 patients were irradiated for nonmalignant diseases annually, which is a significant increase compared to 20,082 patients (+86.2%) anually during the period 1994–1996. The number of patients treated annually within the different disease categories were as follows [numbers in rectangular brackets compare to numbers of patients treated annually in the same categories during the period 1994–1996]: 503 patients (1.3%) with *inflammatory* disorders [456 (2%); +10.3%]; 23,752 patients (63.5%) with *degenerative* disorders [12,600 (63%); +88.5%]; 1,252 patients (3.3%) with *hyperproliferative* disorders [927 (5%); +34.1%], 11,051 patients (29.5%) with *functional*, other or unspecified disorders [6,099 (30%); +81.2%]. 734 patients received stereotactic radiotherapy (SRT) for various nonmalignant disorders such as arteriovenous malformations, meningiomas, acoustic neurinomas/vestibular schwannomas, pituitary adenomas, or other disorders (n = 21; 2%); by comparison, 155 patients were assessed for these disorders during the period 1994–1996.

Other rare diseases reported in the survey of 2001–2002 were pigmented villonodular synovitis (n = 20 patients), vertebral hemangioma (n = 68 patients), and nonmalignant skin disorders (n = 28 patients). The number of patients in each disease category and the institutional type are compared and related to each other in Table 2. Obviously, the increase of patients in the time period of 2001–2002 (+17,328 patients; +86.3%) compared to the time period of 1994–1996 is much more attributed to the community hospitals (+8,969 patients; +57.7%) and private RT centers than university hospitals (+704 patients; +15.5%).

Specific Disease Indications

Patients treated for *inflammatory diseases* (n = 503) included the following disorders: unspecified local inflammatory disorders (n = 240; 48%); sweat gland abscesses or hidradenitis axillaris (n = 204; 41%); infection of the fingernail bed (n = 59; 11%). Although the total number has slightly increased (n = 47; +10.3%), the acceptance of this indication is slowly fading away, even in East German RT institutions.

Patients treated for *degenerative diseases* (n = 23,752) included the following disorders: periarthropathia humeroscapularis (PHS; n = 4,904; +80.9%); epicondylopathia humeri radialis or ulnaris (EPH; n = 3,455; +122.2%); calcaneodynia including plantar or dorsal heel spur (n = 5,971; + 332.1%); other insertion tendinopathy (n = 203; no comparison available); and activated painful osteoarthrosis of various joints (n = 9,219; +278.8%). The number of patients treated in the East German and in private RT centers were significantly higher than those treated in West German and community or university RT institutions.

Patients treated for *hyperproliferative diseases* (n = 1,252) included the following disorders: Dupuytren's disease or Ledderhose's contracture (n = 560; +283.6%); keloids (n = 391; +2.4%); Peyronie's disease (n = 205; +32.3%); pterygium of the eye (n = 56; no comparison); and other disorders without specification (n = 40). The acceptance of this RT indication and the number of patients treated were well balanced between RT institutions and geographic regions in Germany.

Patients treated for *functional and other diseases* (n = 11,051) included different disease groups: Graves' orbitopathy (n = 812; –4.8%); gynecomastia (n = 1,984; no comparison); age-related macular degeneration (n = 259, –74.0%), lymph fistula (n = 161; no comparison); prophylactic RT for the prevention of heterotopic ossification about the hip and other joints (n = 6,637; +80.4%); prophylactic intravascular RT for the prevention of in-stent restenosis after balloon dilatation within coronary arteries (n = 950; no comparison) and within peripheral arteries (n = 248; no comparison). The acceptance of this indication and the number of patients were similar in all RT institutions with the exception of heterotopic ossification prophylaxis which was significantly less implemented in university hospitals regardless of the geographic region ($p < 0.05$) and intravascular RT which was significantly less implemented in private RT centers ($p < 0.05$).

Patients treated with *SRT for various diseases* (n = 744) included the following disorders: arteriovenous malformations (n = 105; 14%); meningiomas (n = 282; 38%); acoustic neurinomas/vestibular schwannomas (n = 168; 23%); pituitary adenomas (n = 168; 23%); or other benign disorders of the brain (n = 21; 2%). The acceptance of this indication and the number of patients treated were significantly higher in university hospitals than in any other institutional type ($p < 0.05$). This was also clearly related to the availability of the technical equipment for SRT and established skills.

Table 2. Different disease categories and institutional type. COM: community hospitals; NA: not available; PRIV: private radiotherapy centers; UNI: university hospitals.

Tabelle 2. Krankheitskategorien und Institution. COM: Versorgungskrankenhaus; NA: nicht verfügbar; PRIV: private Praxen; UNI: Universitätskliniken.

Time period	**1994–1996**			**2001–2002**			
Institution type	**UNI**	**COM**	**Subtotal**	**UNI**	**COM**	**PRIV**	**Subtotal**
Disease category							
Inflammatory Dx	80	376	456	84	350	69	503
Degenerative Dx	1,974	10,626	12,600	2,552	15,202	5,998	23,752
Hyperproliferative Dx	325	602	927	190	787	275	1,252
Functional and other Dx	2,167	3,932	6,099	1,697	7,858	1,082	10,637
Stereotactic Dx	NA	NA	155*	585	140	9	734
Rare Dx	–	–	–	50	59	9	118
Unspecified Dx	–	–	–	92	109	213	414
Overall total	4,546	15,536	20,082	5,250 + 704 (+ 15.5%)	24,505 + 8,969 (+ 57.7%)	7,655 – –	37,410 + 17,328 (+ 86.3%)

* not included in "overall total"

Treatment Concepts

All specified treatment concepts were compared with the recommended national consensus guidelines and with regard to the applied single and total doses, fractionation, and RT technique (Table 3). As not all institutions specified their details, only a portion of all institutions (124; 85%) were included in this analysis. When using megavoltage equipment most institutions (112; 90.3%) specified the target dose to the clinical target volume, but when using the orthovoltage units the majority of all institutions preferred the skin or surface dose prescription (51 of 78; 65%). Only five of 146 RT institutions (3.4%) had to be approached for noncompliance with the consensus guidelines as compared to 36 of 134 RT institutions (26.9%) in the former PCS.

Discussion

Our second national PCS reveals, that many more patients with nonmalignant diseases than 6–7 years ago are treated with RT in Germany. The previously heterogeneous profile of acceptance depending on geographic region and institutional type is diminishing. A few differences are still explained by "old tradition", e.g., inflammatory disorders, or limited availability of RT equipment, e.g., use of SRT. In contrast to the former period, nowadays most RT prescriptions (single/total dose, fractionation schedule, RT technique) comply with published national consensus guidelines [16]. This has also been shown in various other national PCS dealing with specific diseases (Table 1). Nevertheless, still only a small proportion of RT institutions is recruiting patients for prospectively controlled clinical studies (about 14%). Such trials are required to prove the efficacy of RT compared to other therapies and to optimize current RT concepts. The goal is to achieve the best therapeutic effect with an RT concept as economic, as short in time and as low in RT dose as possible.

The European and international medical communities require an evidence-based medicine (EBM) approach for most RT indications, especially for large-scale nonmalignant disorders such as painful joints or insertion tendinitis; these

Table 3. Radiotherapy (RT) concepts for various nonmalignant diseases. AVMs: arteriovenous malformations; E: electrons 4–21 MeV; O: orthovoltage 120–300 kV; P: photons 4–15 MV.

Tabelle 3. Radiotherapie-(RT-)Konzepte für verschiedene nichtmaligne Erkrankungen. AVMs: arteriovenöse Malformationen; E: Elektronen 4–21 MeV; O: Orthovolt 120–300 kV; P: Photonen 4–15 MV.

Diagnosis	Radiation technique	Single dose (Gy)	Total dose (Gy)	Fraction schedule	Treatment time
Local infections, abscess (skin)	O/E	0.2–2.0	a) 0.6–5.0 b) 3.0–10	a) Acute: daily RT: 4–5×/week b) Hypofractionated RT: 2–3×/week	a) 1–3 weeks b) 4–8 weeks
Painful joints: arthritis, bursitis, synovitis	O/E/P	0.3–1.0	a) 3.0–5.0 b) 6.0–12	a) Acute: daily RT: 4–5×/week b) Chronic: hypofractionated RT	a) 2–3 weeks b) Possibly 2nd RT series after 4–8 weeks
Painful joints: insertion tendinitis	O/E/P	0.3–1.0	a) 3.0–5.0 b) 6.0–12	a) Acute: daily RT: 4–5×/week b) Chronic: hypofractionated RT	a) 2–3 weeks b) Possibly 2nd RT series after 4–8 weeks
Desmoids/aggressive fibromatosis	O/E/P	1.8–3.0	a) 50 (R0) b) 60 (R1–2)	Conventional RT: 4–5×/week	a) 5–6 weeks b) 6–7 weeks
Keloids	O/E/P	2.0–5.0	10–21	Conventional RT: 4–5×/week	1–2 weeks, short postoperative interval
Pterygium of the eye	E/strontium applicators	a) 2.0–5.0 b) 10–15	a) 10–21 b) 10–15	a) Conventional RT: 4–5×/week b) Single application	1–2 weeks, short postoperative interval
Dupuytren's disease, Ledderhose's contracture	O/E	2.0–4.0	20–40	a) Conventional RT: 4–5×/week b) Hypofractionated RT: 2–3×/week	a) 2–3 weeks b) Possibly 2nd RT series after 4–8 weeks
Peyronie's disease (plastic induration of penis)	O/E	2.0–4.0	20–40	a) Conventional RT: 4–5×/week b) Hypofractionated RT: 2–3×/week	2–8 weeks
Heterotopic ossification (hip/others)	P	a) 6.0–8.0 b) 2.0–3.0	a) 6.0–8.0 b) 8.0–20	a) Single RT pre-/postoperatively b) Conventional RT: 3–5×/week	a) 1 day pre-/postoperatively b) 5 days, short postoperative interval (24–48 hours)
Graves' orbitopathy	P	1.5–2.0	10–20	Conventional RT: 5×/week	a) 8.0–12 Gy/1 week b) 12–20 Gy/2 weeks
Langerhans histiocytosis/ histiocytosis X	P	1.5–4.0	6.0–20	a) Conventional RT b) Hypofractionated RT: 2–3×/week	a) 1–2 days b) 1–2 weeks
Gynecomastia	O/E	2.0–5.0	a) 12–20 b) 20–30	a) Prophylactic RT b) Therapeutic RT	a) 3–4 days b) 2–3 weeks
AVMs and other vascular malformations	P/stereotactic RT	a) 10–15 b) 2.0–3.0	a) 10–15 b) 45–50	a) Single-dose RT b) Hypofractionated/conventional RT	a) 1 day b) 3–5 weeks

diseases are usually not life-threatening and other treatments are easily available. Financial resources of RT and worldwide acceptance would increase significantly, if successful clinical trials would have been conducted as shown for hyperproliferation prophylaxis for in-stent restenosis [2] and heterotopic ossification [4, 10, 11, 31, 34]. As about one third of 120,000 patients anually undergo total hip arthroplasty in Germany and develop heterotopic ossification, > 30,000 patients may benefit from prophylactic measures including perioperative RT.

A decreasing number of patients are treated with orthovoltage units due to lack of these devices and appropriate substitution by new machines. An increasing shift to megavoltage units has already taken place. As reimbursement for RT of nonmalignant diseases is low, the application with megavoltage units could make this treatment unprofitable, unless reimbursement is improved. Thus, machine capacities for patients with nonmalignant diseases could be compromised in the long-term development. An improved fee structure and technical infrastructure of RT institutions would be beneficial to keep RT of nonmalignant diseases at a high level.

Basic research is required to analyze the effects of low radiation doses on the cytokine cascade, the intercellular contact, the alteration of inflammatory or proliferative reactions and the induction of enzymatic reactions, etc. [8, 26]. Older controlled studies of RT for nonmalignant disorders have been inadequate due to lack of state-of-the-art scientific methods, i.e., lack of appropriate study design, inadequate definition of inclusion and exclusion criteria, incomplete consideration of confounding factors, lack of prospective long-term evaluation and adequate endpoints [3, 23, 38]. Graves' orbitopathy [15, 24] and heterotopic ossification prophylaxis [4, 10, 11, 31, 34] are good examples of improved clinical efforts and clinical studies, as RT for nonmalignant diseases will only be broadly accepted if a favorable risk/benefit ratio is established.

Nonmalignant disorders require a risk versus benefit evaluation for different therapeutic options. For example, about 30% of high-risk patients require prophylactic measures such as nonsteroidal anti-inflammatory drugs (NSAIDs) or perioperative RT to prevent heterotopic ossification after hip surgery. Both methods offer a better outcome, i.e., less ossification and improved hip function, as compared to no treatment (control group) [10, 11]. Regarding patient's compliance and treatment toxicity, prophylactic RT has advantages over NSAIDs in the elderly patient with gastrointestinal risks, while NSAIDs are more easily available than RT and more appropriate for compliant younger patients. While primary costs are obviously more expensive for RT compared to NSAIDs, inclusion of secondary costs due to complications provides a slim advantage for RT over NSAIDs.

In prospective clinical studies the use of subjective evaluation criteria is insufficient to define the effect of RT compared to other therapies. Orthopedics and radiology offer objective scores to measure functional and radiologic changes during the evolution of many orthopedic diseases. In addition, visual analog scales (VAS) quantify subjective criteria such as pain or daily function, while quality of life can be analyzed using the validated SF-36 score. Some of the objective criteria and complex scores have been included in prospective clinical studies dealing with nonmalignant disorders [9, 29, 30, 32]. The implementation of internationally accepted subjective and objective response criteria for validation of treatment outcome within our professional RT community will allow the interdisciplinary design and conduct of multicenter studies within Germany and on an international level. Positive results from these multicenter studies will set preconditions for a broad acceptance of RT for nonmalignant diseases in the whole medical community. For rare nonmalignant disorders the GCG-BD has recently set up several special disease-specific registries to collect clinical data from single institutions to provide a long-term database for better clinical judgment, selection of appropriate treatment concepts, and prognostic guidance on potential clinical outcome [6, 22, 35] (Table 4).

It is also important to warrant follow-up over many years to evaluate late effects and long-term outcome of RT for nonmalignant diseases, as concerns about tumor and leukemia induction will still be arguments against using RT instead of other "less harmful methods".

Table 4. National registries for radiotherapy of rare nonmalignant diseases.

Tabelle 4. Nationale Register für Radiotherapie seltener nichtmaligner Erkrankungen.

Disease group	Status	Coordinator
Kasabach-Merritt syndrome	Activated	Stefan Hesselmann (Münster, Germany) [6]
Extramedullary hematopoiesis	Activated	Oliver Micke (Münster, Germany) [22]
Langerhans cell histiocytosis	Activated	Thomas Olschewski (Essen, Germany) [35]
Gorham-Stout syndrome	Activated	Frank Bruns (Hannover, Germany)
Desmoid (aggressive fibromatosis)	Activated	Oliver Micke (Münster, Germany)
Vertebral hemangioma	In preparation	Oliver Micke (Münster, Germany)
Pigmented villonodular synovitis (PVNS)	In preparation	Hans Eich (Cologne, Germany)
Pseudotumor orbitae (inflammatory pseudotumor)	In preparation	Markus Notter (Aarau, Switzerland)
Neurosarkoidose	Planned	NN

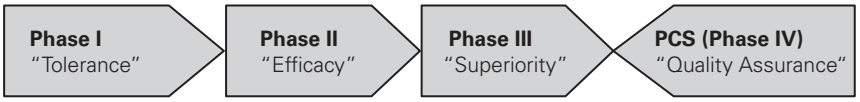

Figure 1a. Patterns-of-care studies (PCS) as an instrument of quality assurance (Model A).

Abbildung 1a. Patterns-of-Care-Studien als Instrument der Qualitätssicherung (Modell A).

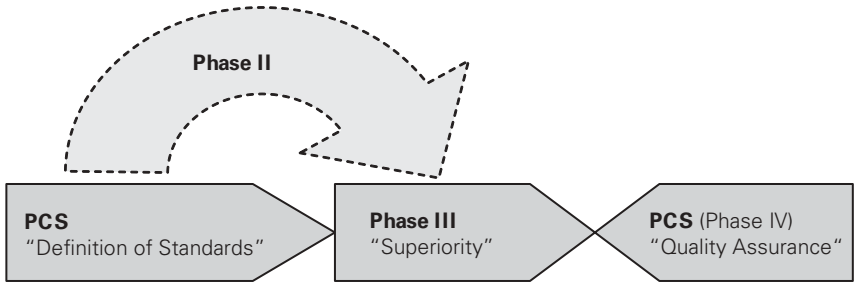

Figure 1b. Patterns-of-care studies (PCS) as an instrument of quality assurance (Model B).

Abbildung 1b. Patterns-of-Care-Studien als Instrument der Qualitätssicherung (Modell B).

Since their first implementation in the USA in 1973, PCS have been a valuable instrument for periodic evaluation of RT practice. Their specific importance is the evaluation of the structure, the processes and, if possible, the treatment outcome [1]. The founder of the Radiation Therapy Oncology Group (RTOG) and the initiator of PCS, Simon Kramer, stated: Patterns of care studies are implemented … *"to improve the quality and accessibility of radiation care in the United States. To this end the PCS seeks to establish how and by whom radiation therapy is being practised in the United States and to evaluate the factors, which affect the levels of care presently being delivered."* [12]. Since these first steps the evaluation of treatment quality has become a very important issue in all medical fields, especially for interdisciplinary cooperation in multimodality treatment concepts required for RT of malignant and nonmalignant diseases [1, 5].

Nowadays, PCS could be applied as a continuous or periodic QA tool similar to the evaluation of a phase IV multicenter study [18] (Figure 1a).

For rare disorders with no or low evidence level, PCS can obtain the role of phase I, possibly phase II clinical trials, as they help to define a commonly practiced RT concept. This may be the starting point for prospectively randomized clinical studies (phase III; Figure 1b).

Summary and Conclusion

PCS are very effective methods to evaluate different clinical indications for RT of nonmalignant diseases. The GCG-BD has successfully conducted and published seven PCS. Additional PCS and registries for rare nonmalignant diseases are planned, e.g., for Langerhans cell histiocytosis, gonarthrosis and vertebral hemangioma, and Peyronie's disease (plastic induration of penis). In Germany in the past decade, RT of nonmalignant disease has been developed with great success, but its general place and purpose in medicine have to be prepared for potential innovative treatment approaches. The presented data allow to derive the following considerations and perspectives:

(1) Structure: most German radiation facilities – regardless of orthovoltage, megavoltage and brachytherapy units – need modernized equipment. In RT departments, which are presently focused only on tumor therapy, the potential patient load has to be carefully calculated to account for the time and personnel required for nonmalignant disorders. Careful documentation and long-term follow-up is an important requirement for QA.
(2) Process: training of medical students and continuous medical education for physicians, i.e., radiologists and radiation oncologists, have to consider new indications, treatment concepts, and implementation of older and modern RT concepts for nonmalignant diseases; interdisciplinary cooperation has to be improved.
(3) Process: technical and clinical QA criteria have to be further developed, and treatment guidelines for RT of nonmalignant diseases have to be continuously reevaluated, if necessary.
(4) Outcome: basic research has to be strengthened, and controlled clinical multicenter studies have to be conducted not only to confirm basic research data, but also to prove treatment efficacy and optimize treatment schedules in "traditional indications" (single/total dose, fractionation).
(5) The economic basis and reimbursement for RT of nonmalignant diseases has to be improved, to avoid negligence of this treatment option among radiotherapists due to economic reasons.

Appendix

1

DEGRO-AG "RT bei nicht-malignen Erkrankungen" 2003

Patterns of Care Studie der DEGRO-AG unterstützt von DEGRO und QRO

1. Allgemeine Daten (bitte auch Telefon/Fax/E-mail für Kontaktaufnahme angeben!)

Klinik/Institution: [ ] Praxis [ ] Versorgungskrankenhaus
[ ] Universitätsklinik [ ] Sonstige Institution

(Adresse) .....

.....

Ansprechpartner: .....Tel./Fax:.....

2. Geräte & Ausstattung (bitte Hersteller und das Jahr der Erstaufstellung angeben !)

Orthovolt < 100 kV [ ] Anzahl/Typ: ..... Jahr: .....

Orthovolt > 100 kV [ ] Anzahl/Typ: ..... Jahr: .....

Elektr. bis ..... MeV [ ] Anzahl/Gerät: ..... Jahr: .....

Photon. bis ..... MV [ ] Anzahl/Gerät: ..... Jahr: .....

3. Personal & Schulung (z.B. Teilnahme an Spezialfortbildungen, Refresher-Kursen!)

Speziell geschulte MTRA [ ] Anzahl; Spezielle Schulung: .....

Speziell geschulte Ärzte [ ] Anzahl; Spezielle Schulung: .....

4. Patienten pro Jahr (speziell 2001 oder 2002)

Nicht-maligne Fälle gesamt [ ] Fallzahl: ..... [ ] Gesamt-Zielvolumina: .....

Maligne Fälle gesamt [ ] Fallzahl: ..... [ ] Gesamt-Zielvolumina: .....

5. Klinische Konzepte & Indikationen (speziell in den Jahren 2001 oder 2002)

Spezialsprechstunde [ ] Tage/Woche: .....

Spezialaufklärung [ ] welche Krankheiten: .....

.....

Spezielle Studien [ ] welche Krankheiten: .....

.....

Eigene Publikationen [ ] welche: .....
(evtl. Kopie dazu!)

.....

Post/Fax: Prof. Dr. med. M.H. Seegenschmiedt, Klinik für Radioonkologie & Strahlentherapie, Alfried Krupp Krankenhaus, 45117 Essen Tel. 0201 / 434 2559 / Fax: 0201 / 434 2371

2

Besondere RT-Konzepte (Bitte nur solche angeben, bei denen auch **aktuelle klinische Erfahrungen** vorliegen!)

Nicht-maligne Erkrankung ....; ICD-10 Nr. ....

Zielvolumen: ....; Dosierungspunkt: ....

Technik: .... kV; Energie .... mA; Filterung ....; Feldgröße .... × .... cm

Einzeldosis: ....Gy; Fraktionen: .... pro Woche; Gesamtdosis: .... Gy

Besonderheiten: ....

....

....

....

Nicht-maligne Erkrankung ....; ICD-10 Nr. ....

Zielvolumen: ....; Dosierungspunkt: ....

Technik: .... kV; Energie .... mA; Filterung ....; Feldgröße .... × .... cm

Einzeldosis: ....Gy; Fraktionen: .... pro Woche; Gesamtdosis: .... Gy

Besonderheiten: ....

....

....

....

Nicht-maligne Erkrankung ....; ICD-10 Nr. ....

Zielvolumen: ....; Dosierungspunkt: ....

Technik: .... kV; Energie .... mA; Filterung ....; Feldgröße .... × .... cm

Einzeldosis: ....Gy; Fraktionen: .... pro Woche; Gesamtdosis: .... Gy

Besonderheiten: ....

....

....

....

Etablierte Indikationen zur Radiotherapie bei nicht-malignen Erkrankungen

BITTE NUR DIE FELDER ANKREUZEN DIE AKTUELL ZUTREFFEN!

1. Entzündliche Erkrankungen

- ☐ **Akute/chronische Entzündungsprozesse**
  Schweißdrüsenabszess, Furunkel, Karbunkel, Nagelbettentzündung

2. Degenerative Erkrankungen

- ☐ **Schmerzhafte Insertionstendinopathie**
  Periarthropathia humeroscapularis (PHS), Epiconylopathia humeri (EPH) radialis/ulnaris, Calcaneodynie, plantarer oder dorsaler Fersensporn
- ☐ **Schmerzhafte degenerative Gelenkerkrankungen**
  schmerzhafte Osteoarthrose von Hüfte (Coxarthrose), Knie (Gonarthrose), Schulter (Omarthrose), Finger-/Daumengelenken (Poly-/Rhizarthrose) u.a.

3. Hypertrophische/hyperproliferative Erkrankungen

- ☐ **Morbus Dupuytren/Morbus Ledderhose**
  im Frühstadium bei Knoten-/Strangbildung ohne Streckdefizit
- ☐ **Morbus Peyronie (Induratio penis plastica)**
  im Frühstadium bei Knoten- und Strangbildung und leichter Penisdeviation
- ☐ **Keloid an der Haut und Pterygium an der Bindehaut des Auges**
  postoperative Vermeidung eines erneuten Rezidivs

4. Funktionelle Erkrankungen

- ☐ **Gynäkomastie**
  Prophylaxe/Therapie schmerzhafter Brustvergrößerung bei Hormontherapie
- ☐ **Endokrine Orbitopathie**
  Vermeidung von Sehstörungen (u.a. Doppelbildern, Visusverlust)
- ☐ **Altersbedingte (feuchte) Makuladegeneration**
  Bestrahlung von Retina/subretinalem Gewebe zum Visuserhalt
- ☐ **Lymphfisteln/Lymphozelen**
  Persistierende Lymphfisteln nach OP in verschiedenen Körperregionen
- ☐ **Prophylaxe heterotoper Ossifikationen**
  Vermeidung von Verknöcherungen nach Trauma/OP an großen Gelenken: Hüfte, Knie, Schulter, Ellenbogen, andere Gelenke oder bei Narbenknochen
- ☐ **Intravaskuläre Bestrahlung koronarer und peripherer Arterien**
  Vorbeugung einer Restenose durch Intimahyperplasie nach Ballondilatation oder Stent-Implantation an den koronaren oder peripheren arteriellen Gefäßen
- ☐ **Stereotaktische Bestrahlung von gutartigen Prozessen im Gehirn**
  Behandlung und Vorbeugung von Rezidiven bei Meningeom, Akustikus-neurinom, Hypophysenadenom, Angiom bzw. Gefäßmißbildungen

5. Weitere Indikationen

- ☐ Pigmentierte villonodöse Synovitis
- ☐ Wirbelsäulenhämangiom; aneurysmatische Knochenzyste; u.a.
- ☐ Hauterkrankungen, z.B. juckende Dermatosen/Ekzeme; Herde bei Psoriasis

DEGRO-AG "RT bei nicht-malignen Erkrankungen" 2003

Patterns of Care Studie der DEGRO-AG unterstützt von DEGRO und QRO

BITTE NUR DIE FELDER ANKREUZEN DIE AKTUELL ZUTREFFEN

Institution:	Fallzahl RT-Konzept (ED/F/GD)
1. Entzündliche Erkrankungen gesamt	[ ] ED F GD
[ ] **Entzündungsprozess (akut/chronisch)**	[ ] ..... Gy × ..... = ... Gy
[ ] Schweißdrüsenabszesse, Furunkel, Karbunkel	[ ] ..... Gy × ..... = ... Gy
[ ] Nagelbettentzündung (Panaritium; Paronychie)	[ ] ..... Gy × ..... = ... Gy
2. Degenerative Erkrankungen gesamt	[ ] ED F GD
[ ] **Insertionstendinopathie (akut/chronisch)**	[ ] ..... Gy × ..... = ... Gy
[ ] Periarthropathia humeroscapularis (PHS)	[ ] ..... Gy × ..... = ... Gy
[ ] Epiconylopathia humeri (EPH) rad./uln.	[ ] ..... Gy × ..... = ... Gy
[ ] Calcaneodynie/Fersensporn plantar o. dorsal	[ ] ..... Gy × ..... = ... Gy
[ ] **Gelenkerkrankungen (akut/chronisch)**	[ ] ..... Gy × ..... = ... Gy
[ ] Osteoarthrose der **Hüfte** (Coxarthrose)	[ ] ..... Gy × ..... = ... Gy
[ ] Osteoarthrose des **Knies** (Gonarthrose)	[ ] ..... Gy × ..... = ... Gy
[ ] Osteoarthrose der **Schulter** (Omarthrose)	[ ] ..... Gy × ..... = ... Gy
[ ] Osteoarthrose des **Daumens** (Rhizarthrose)	[ ] ..... Gy × ..... = ... Gy
[ ] Osteoarthrose der **Finger** (Polyarthrose)	[ ] ..... Gy × ..... = ... Gy
[ ] **Sonstige Arthrosen** an anderen Gelenken	[ ] ..... Gy × ..... = ... Gy
3. Hyperproliferative Erkrankungen	[ ] ED F GD
[ ] **Morbus Dupuytren** (im Frühstadium)	[ ] ..... Gy × ..... = ... Gy
[ ] **Morbus Ledderhose** (im Frühstadium)	[ ] ..... Gy × ..... = ... Gy
[ ] **Morbus Peyronie (IPP)** (im Frühstadium)	[ ] ..... Gy × ..... = ... Gy
[ ] **Keloid der Haut**	[ ] ..... Gy × ..... = ... Gy
[ ] **Pterygium der Bindehaut** (postoperativ)	[ ] ..... Gy × ..... = ... Gy
[ ] **Sonstige hyperproliferative KH** welche:	[ ] ..... Gy × ..... = ... Gy

Institution:	Fallzahl	RT-Konzept (ED/F/GD)
4. Funktionelle Erkrankungen gesamt	[ ]	ED F GD
[ ] Gynäkomastie (Prophylaxe/Therapie)	[ ]	..... Gy × ..... = ... Gy
[ ] Endokrine Orbitopathie (Kategorie III–VI)	[ ]	..... Gy × ..... = ... Gy
[ ] Altersbedingte Makuladegeneration	[ ]	..... Gy × ..... = ... Gy
[ ] Lymphfisteln/Lymphozelen	[ ]	..... Gy × ..... = ... Gy
[ ] Prophylaxe heterotoper Ossifikationen	[ ]	..... Gy × ..... = ... Gy
[ ] Intravaskuläre Bestrahlung In-Stent Restenose in koronaren Arterien	[ ]	..... Gy × ..... = ... Gy
[ ] Intravaskuläre Bestrahlung In-Stent Restenose in peripheren Arterien	[ ]	..... Gy × ..... = ... Gy
5. Stereotaktische RT – ZNS gesamt	[ ]	ED F GD
[ ] Angiome/arteriovenöse Malformation	[ ]	..... Gy × ..... = ... Gy
[ ] Meningeom/Meningeom-Rezidiv	[ ]	..... Gy × ..... = ... Gy
[ ] Akustikus-Neurinom/-Rezidiv	[ ]	..... Gy × ..... = ... Gy
[ ] Hypophysenadenom/-Rezidiv	[ ]	..... Gy × ..... = ... Gy
[ ] Andere gutartige Prozesse im ZNS welche:	[ ]	..... Gy × ..... = ... Gy
6. Seltene weitere Indikationen gesamt	[ ]	ED F GD
[ ] Pigmentierte villonodöse Synovitis	[ ]	..... Gy × ..... = ... Gy
[ ] Hämangiom der Wirbelsäule	[ ]	..... Gy × ..... = ... Gy
[ ] Gutartige Hauterkrankungen z.B. juckende Dermatosen/Ekzeme	[ ]	..... Gy × ..... = ... Gy
etc.		
etc.		(Bitte beiliegende Blankobögen verwenden !)
Gesamt 2001 oder 2002 (Summe Nr. 1–6)	[ ]	/Kommentar:

BITTE NUR DIE FELDER ANKREUZEN DIE AKTUELL ZUTREFFEN

Post/Fax : Prof. Dr. med. M.H. Seegenschmiedt
Klinik für Radioonkologie und Strahlentherapie
Alfried Krupp Krankenhaus, 45117 Essen
Tel. 0201 / 434 2559 / Fax: 0201 / 434 2371

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Address for Correspondence
Professor M. Heinrich Seegenschmiedt
Department of Radiation Oncology and Radiation Therapy
Alfried Krupp Hospital
Alfried-Krupp-Straße 21
45117 Essen
Germany
Phone (+49/201) 434-2560, Fax -2371
e-mail: heinrich.seegenschmiedt@krupp-krankenhaus.de