BenigNews

Founded in 2000

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

Inside this Issue:

Editor's Corner

Dear Colleagues and Friends of Radiation Medicine,

Our new LOGO for **BenigN**[ews] can be seen for the first time on the right top front page. With a little imagination the three letters, "R" for radiotherapy, "B" for benign and "D" for diseases, can be found between three bending arrows and three beaming triangles. As in oncology the three arrows symbolize the different approaches that meet this specialized medical field: pharmacology, surgery and radiotherapy. While drugs and surgery are sometimes limited or may not be the treatment of choice for the patient, the third option - radiation therapy - offers a possible alternative.

Without doubt, interdisciplinary cooperation in the various medical fields is the corner-stone for the successful application of radiation therapy for benign diseases. Without understanding the point of view of other specialists, e.g. the orthopedic surgeon or the cardiologist, radiotherapists will have a difficult time communicating their treatment options and how they can impact on the clinical indication process. Thus, it will be very important to have a professional basis for all interdisciplinary applications of ionizing radiation. Few in our field would like to lose the newly developed field of cardiovascular or peripheral arterial radiotherapy to other specialists who do know less of radiation biology, radiation physics and potential benefits and hazards of clinical radiotherapy applications.

In this issue we are advertising the internet version of **BenigNews**, which has been available since October 2000. It has already received more than 1.000 hits. We would like to encourage comments and proposals for improvement of our internet version.
A report from the recent ASTRO conference in Boston summarized the various refresher courses, panels and papers which were presented on topics dealing with radiotherapy for benign diseases. The papers addressed several topics of clinical and biological aspects of "Radiotherapy for Benign Diseases". The fact that these oral and poster presentations were well accepted, demonstrates a successful track for our field. Other topics presented in this issue include the recent advances in vascular radiation medicine and a report of prophylactic irradiation in patients with resected keloids.

Again, **BenigN**[ews] contains special forms for documentation and evaluation of radiotherapy for painful joints including painful degenerative osteoarthritis and insertion tendinitis at various body sites. We will continue to present these tools in upcoming issues. This should help to structure clinical work including documentation and evaluation and promote future prospective clinical research. Additional suggestions and improvements are always welcome; we would appreciate the appropriate citation of these documentation forms when they are applied in clinical trials. This issue is concluded with a rare case report on a successful treatment of a Gorham-Stout syndrome with massive osteolysis of the cervical spine.

Our calendar has dates of several scientific conferences occurring in 2001 and which include radiotherapy of benign diseases. One is the 4th Annual Meeting of the German Cooperative Group on "Radiotherapy for Benign Diseases" which will take place on May 4 - 5, 2001 in Essen. Hopefully in 2002 or 2003 we will , in partnership with ESTRO , schedule the 2nd European Conference on Benign Diseases. For the next **BenigN**[ews] we would appreciate further conversation, comments and suggestions from all readers of the upcoming issues by via phone, fax, internet or personal communication. Sincerely Yours,

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& Hans-Bruno Makoski, Duisburg (Germany)

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Benign News from the Net – The World Wide Web and the Benign Diseases

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Only two decades ago, supplying the right information in the right places was simply a question of what to print in which journal or newsletter. With the ever increasing omnipresence of new media e.g. television, CD-ROM, DVD, and last but not least the Internet and the World Wide Web, the old ways of communication have changed drastically (1). This change influences the channels of information for the private household as well as for business and government use, but it also affects the scientific community in an inspiring and fascinating way (2, 4).

For example, for a literature overview it is no longer necessary to go to the library, search through the catalogues, and look for the corresponding journals etc. (which frequently takes hours). Instead, a short look into Medline or PubMed yields thousands of references (or just two, it's your choice), complete with abstracts. In most cases, the whole article can be retrieved in full text and printed on your home or office printer without even having to move from your chair (3, 4). And via e-mail, in only a few seconds more, you can send a note on your new findings to your colleague on the other side of the globe, possibly including some important diagrams as an attachment (3).

The widespread use of the internet has also influenced the ways of patient information. In a recent survey in Germany, a total of 26.6% of cancer patients received information on their disease directly or indirectly from the internet (6). This was especially in younger age patients, those with a higher education, and for palliative patients, where the rates of internet use were substantially higher and the use of electronic media is rapidly growing.

All these new means of communication and information retrieval influence the way a scientific working group should present itself to the public. Recently we have shown that it is possible to set up a low cost website and provide current information on the field of trace elements and electrolytes (5). The site has received over 1000 hits so far.

Of course, there will always remain the conventional way of publishing scientific findings in scientific journals and newsletters like BenigNews, but the world is changing rapidly, and up-to-date information can best be provided via an electronic medium like the Internet.

For this reason we have set up a homepage for BenigNews, which can be found at http://www.benign-news.de (Fig. 1).

Fig. 1: Homepage of BenigNews (www.benign-news.de) as of January, 2001

Our homepage currently shows an overview of the first BenigNews issue, as well as full text links to all issues in the free, standardized PDF format (the plug-in program needed can be downloaded for free on the Adobe® homepage). Protocols of working group meetings are also available online. The complete set of instructions for authors for BenigNews can be downloaded as well.

Announcements of important events in the field of radiation therapy for benign diseases will be presented as soon as they become available. Questionnaires and documentation sheets are available online (e.g. the Morbus Dupuytren documentation sheets) as well as tables with important facts like the Excerpt of the ICD-10 Classification for Radiotherapy of Benign Diseases. Finally, we have added a counter showing that our page has received over 300 hits since October 2000.

Additionally, the BenigNews homepage has been submitted to most major search engines (Fig. 2), so that anyone (patient or physician) surfing the internet with an interest in radiation therapy of benign diseases will be able to find us.

Fig. 2: The Google™ search engine (www.google.com) with the keywords "benign diseases radiotherapy". Our site is shown in the third and fourth position

This is the first news from our activity in the Net; hopefully it will be of importance to scientific community and clinical practice alike.

We hope that the reader will find much useful information at our site. Comments on possible improvements are of course always welcome. Correspondence via e-mail is preferred; the email address of the webmaster is: webmaster@benign-news.de or at pschuel@uni-muenster.de.

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Benign News from New England – Report from the 42nd Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) in Boston, October 22-26, 2000

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The annual ASTRO Meeting took place in historic Boston, MA, a city with a fascinating mixture of American historical sites and modern life. History - present and future can be seen side by side.
And, best of all, you can walk everywhere. From European-inspired Beacon Hill to the art galleries and cafes of Newbury Street, every step is unforgettable.
Boston is not only the right place to have good tea parties (Fig. 1) but for scientific meetings too.
Boston is not only one of the best places to have a good tea party (Fig. 1) but also a scientific meeting too.
The meeting place, the John B. Hynes Veterans Memorial Convention Center, is located in heart of Boston's beautiful Back Bay, just steps away from Newbury Street's renowned shops, galleries and restaurants (Fig. 2).

Fig. 1: Historic print of the Boston Tea party, December 16, 1773

Fig. 2: The Hynes Convention Center situated in the nice Back Bay of Boston

With more than 5,000 participants and 523 abstracts presented, the meeting was one of the biggest ASTRO-Meetings ever. Radiotherapy of benign diseases was well represented with a total of 15 Abstracts dealt with non-malignant diseases.

There were four refresher courses on intravascular brachytherapy: Part I: Introduction to interventional techniques and animal studies. (R. Waksmann, Washington Cardiology Center, Washington, DC), Part II: Clinical studies in coronary arteries (P. Tripuraneni, Scripps Clinic, La Jolla, CA), Part III: Clinical studies in peripheral arteries (D. Nori, New York Cornell Hospital, New York, NY, S. Parikh, New York Hospital Medical Center, New York, NY) and Part IV: Physics of intravascular brachytherapy (S.-T. Chiu-Tsao, Beth Israel Medical Center, New York, NY, R.C. Chan, Washington Hospital Center, Washington, DC). P. Tripuraneni predicted in his refresher course the future direction of vascular brachytherapy: "The future for vascular brachytherapy is bright and the results of various clinical trials over the next one to two years will determine the magnitude of its role for patients with coronary vessel disease. Close working relations between Interventional Cardiology and therapeutic Radiology will be crucial for the continued further development of this field both in clinical and research arenas".

In addition there was another refresher course on general treatment aspects of radiotherapy of non-malignant diseases: Radiation therapy for benign disease: **Contemporary concepts and clinical results - Part I** (M.H. Seegenschmiedt, Alfried Krupp Krankenhaus, Essen Germany). eg for the prevention of heterotopic ossifications by ionizing irradiation he stated: "In summary, radiation therapy can be regarded as a prophylactic therapy to prevent heterotopic ossification of any kind." … "Radiobiological and clinical research have to answer several open questions regarding the pathophysiology of these conditions, the target cells and mechanisms of action of ionizing irradiation" … "Moreover, optimal organization of radiotherapy department and economic considerations such as cost-benefit calculations when providing prophylactic treatment for larger groups of patients with non-malignant disorders have to be carefully assessed in the future." Hopefully a part II of this session will follow at the 2001 ASTRO-Meeting in San Francisco.

A panel of Speakers discussed **The Advances in Cardiovascular Radiation Medicine** chaired by P. Rubin (University of Rochester Medical Center, Rochester, NY) and P. Tripuraneni (Scripps Clinic, La Jolla, CA). Panelists were J. Williams (University of Rochester Medical Center, Rochester, NY), I. Crocker (Emory Clinic, Atlanta, GA), H. Arnols (Memorial Sloan Kettering Cancer Center, New York, NY) and R. Waksmann (Washington Cardiology Center, Washington, DC). This session fired the imagination of radiation practitioners and should help to establish the use of radiotherapy for restenosis as a valid form of treatment. Exciting and promising results of randomized clinical trials utilizing vascular brachytherapy to prevent restenosis post angioplasty and stenting in coronary arteries were presented. The scientific basis for the successful use of radiation was provided in terms of the principles of radiation biology and radiation physics established in oncology. The status of FDA approval and reimbursement was also covered.

The scientific program devoted two session to non-malignant diseases. One dealt with intravascular brachytherapy and showed the emerging progress of this treatment option on its way to well accepted and widely used treatment modality (2, 5, 12, 13).
A second session chaired by M. Coleman (University of Texas Medical Branch, Galveston, TX) and M.D. Kelly (University of Virginia School of Medicine, Charlottesville, VA) was held about all others aspects of non-malignant diseases. More than half of the session came from the German group.
O. Micke (University of Münster, Germany) presented on behalf of the German Cooperative Group on "Radiotherapy for Benign Diseases" (GCG-BD) consensus guidelines for radiation therapy of benign diseases, which had been defined in a multi-center approach. For the first time, consensus guidelines for RT of benign diseases have been developed by the interaction of all involved RT institutions. This may serve as a starting point for quality assessment, design of prospective clinical trials and outcome research. It was recommended that an international consensus process should be started to develop an

updated international standard of care using RT for benign conditions (7).
D. Marquez (Stanford University Medical Center) reported 179 patients treated for Graves' eye disease with 20 or 30 Gy and a median follow-up of 59 months. They demonstrated an excellent subjective outcome and patients satisfaction of 98 %.
S. Hesselmann (University of Münster, Germany) presented the results of a long-term follow-up study after retro-orbital irradiation for Graves' ophthalmopathy. They found in this cohort study that, there was no significant evidence of radiation induced death in patients treated with radiotherapy for Graves' eye disease. The long-term results were satisfactory. (4).
M.H. Seegenschmiedt (Alfried-Krupp Krankenhaus Essen, Germany) presented the results of two German patterns of care studies on prophylactic irradiation of heterotopic ossifications of the hip and other body sides besides the hip joint. He demonstrated in this study, with the largest number of cases reported for prophylactic radiotherapy about the hip, that pre- (within 24 hrs) and postoperative radiotherapy (within 96 hrs) is effective for HO prophylaxis and achieve similar radiological and functional response rates. Radiotherapy provides an excellent treatment alternative for patients with contraindications to long-term steroids or NSAID medication (8, 10).
F. Pohl from the University of Wuerzburg, Germany confirmed these results. They showed that the combination of prophylactic irradiation in the evening before total hip replacement with a pain adapted NSAID-therapy reduced the incidence of HO. The results of this combined therapy are comparable to those of a preoperative irradiation 4h before operation or a postoperative irradiation without NSAID-therapy (9).
J.H. Suh (Cleveland Clinic Foundation, Cleveland, OH) presented the results of Gamma knife radiosurgery for trigeminal neuralgia and stated that it is an effective treatment option for patients with newly diagnosed and recurrent trigeminal neuralgia (11).
B. Adamietz (University of Erlangen, Germany) demonstrated in 205 hands treated for early stage Dupuytren's contracture radiotherapy to be a safe and effective treatment (1).
D. Fröhlich (Zentralklinikum Suhl, Germany) presented the results of 252 patients treated for inflammatory diseases of the extremities. He concluded, that radiotherapy is a safe and very efficient method in this patients. With a rate of 81 % patients free of symptoms or clearly improved, antiphlogistic irradiation for panaritium and paronychia is still relevant today. It was possible to avoid the amputation of fingers or toes due to osseous involvement (3).

In conclusion this ASTRO-Meeting reflected the growing interest of the American radiation oncologists in radiotherapy for benign diseases. Intravascular brachytherapy is likely to become a standard treatment after percutaneous coronary or peripheral angioplastic procedures. The impact of external beam is uncertain so far. Other Indications eg irradiation prevention for heterotopic ossifications, irradiation for endocrine orbitopathy or Dupuytren`s Contracture are becaming more acceptable. Other indications need to be tested in clinical studies. When using irradiation for these indications, the possible benefit must be weighed against the potential risks.

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Benign News from the Vessels – Advances in vascular radiotherapy

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It is anticipated that vascular radiation medicine will be practiced as a standard of care for patients with in-stent restenosis vascular brachytherapy with approval for clinical use (5). However, there are unanswered questions, namely, the selection of the ideal isotopes, dosimetry planning, and improvement in methods and devices to deliver the right dose to the target area. The mechanisms of vascular radiation still remain in question. Apoptosis, anti-inflammatory, or anti-angiogenic factors require further investigation and explanation. Furthermore, it requires efforts to minimize complications eg late thrombosis, edge effect, and delayed restenosis.
The main focus of the present and following articles in this journal will be a controversial discussion of selected papers published recently.

Makkar et al. examined the effects of a ß-emitting 188Re-Balloon in stented porcine coronary arteries in an angiographic, intravascular ultrasound, and histomorphometric study (2). One group of animals received 0, 16, 22, or 29 Gy at 0.5-mm depth, followed by stenting. Another group was stented first and then treated with 0 or 29 Gy. Follow-up was 60 days. There was a measurable effect at 16 Gy, which improved with increasing doses. The authors found that radiation was equally effective when given before or after stent placement.
In their brief rapid communication in Circulation in December 2000, GS. Mintz and coworkers described the effect of intracoronary γ-radiation therapy on in-stent restenosis from the Gamma-1 Study (3). In this study, 70 patients were randomized to receive either 192 Ir or placebo after successful restenting. The dwell time was calculated to deliver 800 cGy to the target farthest from the radiation source, provided no more than 3000 cGy. The study was able to demonstrate a significant reduction (in late lumen loss and neointimal hyperplasia in patients with In-Stent Restenosis treated with γ-radiation.
Pokrajac et al have published the results of their prospective randomized Vienna-2-Trial (4). Patients were randomized after successful femoropopliteal percutaneous transluminal angioplasty (PTA) for intraarterial 192IR high-dose-rate brachytherapy versus no further treatment. A dose of 12 Gy was prescribed in 3-mm distance from the source axis. Primary endpoint of the study was femoropopliteal patency after 6 months. A total number of 113 patients was enrolled. After a follow-up of 6 months, a significant reduction of the restenosis rate in the PTA & brachytherapy arm could be demonstrated.

Hehrlein et al. tested a novel balloon angioplasty catheter for vascular brachytherapy (1). Instead of a liquid beta-radiation (Re-188) balloon, the balloon surface of an angioplasty catheter was impregnated with the radioisotope 32-P. In a rabbit model, neointima formation was significant reduced after balloon dilatation and simultaneous beta-particle irradiation compared to balloon dilatation alone with a non-impregnated catheter. The possible advantage of this system could be more security from leakage of liquid filled balloon systems.

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Papers revisited:

Results of Prophylactic Irradiation in Patients with Resected Keloids

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Keloids are the result of a pathological wound healing process, in which the region becomes hypertrophic, with a soft tissue mass developing in the area surrounding the wound - this can extend beyond the former wound margin (Fig. 1).

Fig. 1: Keloid of the forearm after a burning lesion

Like malignancies, keloids have rapid growth phases and phases with little or no growth activity (1, 2).
The maximum extent of the disorder is usually reached 2 - 3 months following the onset of keloid formation (3). Clinically , it can be difficult for the physician in some cases to differentiate between keloids and hypertrophic scars (4, 5, 6).
In the past many different treatment modalities have been used, especially surgical excision. Nevertheless, the recurrence rate after surgery alone is calculated to be as high as 50%-80 % (7-9). Therefore, adjunctive procedures have been proposed in the literature to improve therapeutic outcomes. Intralesional injection of corticosteroids has been widely used, but the published 5-year response rates are only around 50 % (10, 11). Another approach are pressure bandages, but these dressings must be worn for a long time (10).
For postoperative irradiation there numerous references in the literature demonstrating that the side effects rate of this treatment modality is low and the response rates are high (12-14).
There has been considerable turnover of medical investigator staff at our institutes between 1962 and 1997, and the techniques (especially total doses and single doses) have been modified as well. Therefore there is sufficient data to establish a dose response profile for this kind of therapy.

Patients and Methods:

Between 1962 and 1996 a total of 194 patients with keloids were treated postoperatively with Sr-90 brachytherapy at the University of Münster and the Paracelsus-Strahlenklinik, Osnabrück.
As keloids are benign disorders there were no regular follow-up examinations in the institutes and we only were able

evaluate the outcome of therapy using a questionnaire which was send to all patients and then analyzed.

139 patients with 166 keloids answered and in the following only these clientele was taken into consideration.
The median age of the patients was 29 years for the female patients and 20 years for the male patients. In 60 % of all patients, keloids developed before the third decade of life.
85 % of all the keloids had become manifest before the end of the third decade and only 15 % of all treated keloids had developed later in the fourth decade.
Many keloids developed in the region of the anterior thorax (27%). Nearly the same incidence was documented for the facial region (25%), followed by lesions involving the neck (22%) and the abdomen (11%). The rest of the keloids involved the back, extremities, hand and ear.
All keloids were resected, and irradiation was begun within the first 48 hours after resection. Irradiation was carried out using an integrated Sr-90 surface applicator.
The advantage of using contact brachytherapy can be seen in the very minimal invasion depth of the ß-rays. Thus the 80 % isodose penetrates only 2-3 mm below the skin surface.
Most keloids developed following surgical resection (n=66), traumatic lesions (n=45) or burns of different degrees (n=28).
The etiology of the remaining keloids (n=27) was unknown at the time of evaluation. The median extension of the keloids was 6 cm (range: 2 cm - 24 cm).
There were only 5 keloids larger than 10 cm. Keloids which had been larger than the diameter of an applicator were treated using a special handle in which up to 4 applicators could be fixed next to each other.
24 keloids were exposed to a total dose between 7.5 Gy and 10 Gy, 30 keloids between 10.5 Gy and 12 Gy, 36 keloids between 12.5 Gy and 14 Gy, 30 keloids between 15 Gy and 17 Gy, 23 keloids between 18 Gy and 20 Gy, 11 keloids between 21 Gy and 24 Gy and 12 keloids between 26 Gy and 28.5 Gy.
The median single dose was 3 Gy (range 1.5 Gy- 4 Gy). Irradiation was carried out every day except Saturday and Sunday.
The median follow-up was 12 years.
Statistical evaluation was done using chi-square analysis.

Results:

75 % of the patients suffered from pain, discomfort or tension before surgical removal. Only 25 % of all patients were completely symptom-free. 67 % of the patients suffering from symptoms due to keloid formation were female.
85 % of the initially patients were totally symptom-free 6 weeks after the end of combined therapy (resection and irradiation). No change of symptoms was documented in 15 %, but the majority of these patients had developed recurrences at this time. Only 2 patients complained about pain after therapy without any signs of recurrences.
79.5 % of all patients had no evidence of recurrence and we were not able to document a significant difference between male and female patients (82.4 % recurrence-free response rate for the female patients versus 71,8 % recurrence-free response rate for the males). 15 % of all recurrences developed within the first 2 months after therapy, 60 % within 6 months, 76 %

within 12 months and 100 % within 24 months after the end of therapy. We did not find any recurrences later than 2 years after therapy.
Hence, half of all recurrences developed within the first 6 months after therapy. After the end of the first year, about 75 % of all recurrences were manifest.
A correlation between success rates or recurrence rates and total dose was not seen.
There was a significant difference in treatment outcomes in relation to the anatomical region of the keloids.
Patients with keloids in the region of the face and neck had a response rate of nearly 100 % in contrast to patients with disorders in the region of the thorax. At the thorax the response rate was only 51 %, representing a recurrence rate of 49 % ($p<0.001$).
Furthermore we could identify a significant correlation (Table 1) between response rate and etiology. Keloids resulting from burns had a significantly poorer outcome than keloids following surgical intervention or mechanical trauma ($p<0.001$).

Cause of keloids	Total number of keloids	Recurrence-free success rate	Recurrence-rate
Surgery	66	55 (84 %)	11 (16%)
Traumatic lesion	45	33 (74 %)	12 (26%)
Burns	28	9 (32 %)*	19 (68%)*
Unknown	27	24 (88,9%)	3 (11,1%)

* $p < 0.001$

Table 1: Impact of etiology on success rate

There was no significant correlation between response and the duration of the condition, nor was there a correlation between response rate and keloid size.
Keloids present more than 2 years before therapy had a recurrence-free response rate of 78.9 % in comparison to 68.8 % for keloids existing only between 1 and 6 months.
There were no significant difference in outcome in relation to gender and age.
With regard to side effects, acute erythema was seen in 24 % and hypopigmentation in 11 %, and this was especially seen in patients receiving the higher total doses. Presently, no secondary malignancies in the irradiated areas have been reported.

Discussion

Our study identified a response rate of about 80 % after keloid resection and irradiation. As previously stated, this corresponds with other data from literature (9, 15, 16).
We did not identify a significant difference between response rate and total dose in our patient population, suggesting that lower doses of irradiation may be sufficient (8 Gy-10 Gy). This is also reported in the literature (11, 17).
We observed no difference in therapeutic outcome in relation to gender and age. This fact is discussed controversially in literature (11, 14).
Additionally, we documented a significantly different outcome relating to the anatomical site of the keloid. Patients with keloids involving the face and neck had a significantly better response rate than patients with keloid formation on the thorax. This is a point which has not been stressed in the literature in the past.
This may be related to traction forces active in the region of the female breast and the decolleté which can favor the development and recurrence of keloids, but the exact reason for this significant difference remains unclear so far.
We have demonstrated a correlation between keloid aetiology and recurrence.
Keloids following burns had a significantly poorer outcome than keloids developing after mechanical trauma or surgical excision. This might be a new prognostic factor in keloid therapy which should be considered in further studies. The observation that keloid manifestations at the thorax and keloids following burns had a poorer outcome was unrelated to the size of the keloids. We established no significant difference in size between keloids at the face and neck and keloids elsewhere on the body.
Acute side effects as well as late side effects were slight and within the area of irradiation, no evidence of secondary malignancies were detected. This corresponds to the data from literature and emphasizes the important role of this therapy modality (9, 12, 13).

Conclusion

Postoperative irradiation of keloids is an effective therapy modality with few side effects. In our retrospective analysis we were able to confirm some results from other investigators eg independence from total radiation dose, the high overall success rates and the low incidence of acute and late side effects, too. Furthermore, there were no secondary malignancies within the area of irradiation after a long median follow-up time.
In addition to other reports, two new prognostic factors could be identified: The etiology of the keloids and the localization of the disorders.
If other studies could confirm these results, total doses may need to be increased in the thoracic area and perhaps in keloids after burns.

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Painful Joints - Documentation A

Date of 1st Clinical Assessment ⌊ ⌋⌊ ⌋⌊ ⌋

Family Name ..... **Surname** ..... **Date of Birth** ⌊ ⌋⌊ ⌋⌊ ⌋

What is your **body height ?** ……. (cm) What is your **body weight ?** ……. (kg)

Where do you feel pain ? (Body Site) .....

Since when do you have pain ? ⌊ ⌋ 1 - 4 wks; ⌊ ⌋ 1 - 3 mos; ⌊ ⌋ 3 - 6 mos;
⌊ ⌋ 6 - 12 mos; ⌊ ⌋ > 1 year; since ⌊ ⌋ years.

How is the pain characterized ? (exact description)
……

When does the pain occur ? (exact description)
……

In which direction is pain irradiating ? (exact description)
……

Which degree of pain exists ?	**„none“**	**„mild“**	**„moderate“**	**„severe“**
S = Pain at **Strain**	⌊ ⌋ 0	⌊ ⌋ 1	⌊ ⌋ 2	⌊ ⌋ 3
N = Pain at **Night**	⌊ ⌋ 0	⌊ ⌋ 1	⌊ ⌋ 2	⌊ ⌋ 3
P = **Permanent** Pain	⌊ ⌋ 0	⌊ ⌋ 1	⌊ ⌋ 2	⌊ ⌋ 3
R = Pain at **Rest**	⌊ ⌋ 0	⌊ ⌋ 1	⌊ ⌋ 2	⌊ ⌋ 3
F = Pain at **First Movement**	⌊ ⌋ 0	⌊ ⌋ 1	⌊ ⌋ 2	⌊ ⌋ 3

How do you score your pain overall ? (please set cross mark !)

0 **10**
[------i------i------i------i------I------i------i------i------i------]
No Pain > > > > > > > > Most severe Pain

Which symptoms exist ?

Redness of joint(s) ⌊ ⌋ yes ⌊ ⌋ no; **Swelling** of joint(s) ⌊ ⌋ yes ⌊ ⌋ no

Limited motion ⌊ ⌋ yes ⌊ ⌋ no; **Loss of Function** ⌊ ⌋ yes ⌊ ⌋ no

Restricted profession ⌊ ⌋ yes ⌊ ⌋ no; **Restricted Sports** ⌊ ⌋ yes ⌊ ⌋ no

Which profession is / was practiced ?

(professional activities) .....

Which diseases did you have ? (please cross mark if appropriate) **B**

⌊ ⌋ Bone Fracture / Trauma ⌊ ⌋ Infection of Bone / Joint ⌊ ⌋ Chron. Polyarthritis

⌊ ⌋ Diabetes mellitus ⌊ ⌋ Perfusion Disorder ⌊ ⌋ Osteoporosis

⌊ ⌋ Periph. Nerve Disorder ⌊ ⌋ (Para)Thyroid Disorder ⌊ ⌋ Other Disorders:

.....

Have the **pain symptoms /** has the **disease increased** within the past time period ?

⌊ ⌋ **No**; ⌊ ⌋ **Yes**, within … ⌊ ⌋ Weeks ⌊ ⌋ Months ⌊ ⌋ Years

Which physicians did you consult about the pain symptoms / the disorder in the past **?**

⌊ ⌋ Family Practitioner ⌊ ⌋ Medical Specialist (s) / Name :

.....

Which treatments have been conducted in the past ? (please list type of treatment and time)

Type of Treatment :	**Period (from / to):** **Success: Yes [ ] / No [ ]**
Oral Medication Steroids Non-Steroidal Antirheumatics Opioids / Morphin-like drugs Others	Yes [ ] / No [ ]
Physiotherapy (Number, Type of Treatments)	Yes [ ] / No [ ]
Electrotherapy (Number, Type of Treatments)	Yes [ ] / No [ ]
Local Injection (s) Steroids, Anesthesics (Number, Type of Treatments)	Yes [ ] / No [ ]
Local Ointment (s) (Type of Medication)	Yes [ ] / No [ ]
Surgery / Operation (s) (Date, Type of Surgery)	Yes [ ] / No [ ]
Other Treatment (s) (Number, Type of Treatments)	Yes [ ] / No [ ]

Other Notes :

Date,
Signature (Patient) : …….. (Physician): ……..

Physical Examination / Date ⌊ ⌋⌊ ⌋⌊ ⌋ **(prior to RT)** **C**

Involved Joints	**Right Side**					**Left Side**				
Finger (s) No.	**F 1**	**F 2**	**F 3**	**F 4**	**F 5**	**F 5**	**F 4**	**F 3**	**F 2**	**F 1**
DIP / PIP Joint (s)										
MCP Joint (s)										
Wrist										
Elbow										
Shoulder										
Hip Joint										
Knee Joint										
Ankle Joint										
MTP Joint (s)										
DIP / PIP Joint (s)										
Toe (s) No.	**T 1**	**T 2**	**T 3**	**T 4**	**T 5**	**T 5**	**T 4**	**T 3**	**T 2**	**T 1**
Ankylosis										
Swelling / Effusion										
Pressure Pain										
Pain Irradiation										

Tested Functions	**Neutral - Zero - Method**	**Neutral - Zero – Method**
Flexion **Extension**	**…… / 0° / ……**	**…… / 0° / ……**
Internal Rotation **External Rotation**	**…… / 0° / ……**	**…… / 0° / ……**
Abduction **Adduction**	**…… / 0° / ……**	**…… / 0° / ……**
Other Function (s) :	**…… / 0° / ……**	**…… / 0° / ……**
Typical Function (s):		

Legend: **P** = Pressure Pain; **F** ↓ = Reduced Function (% Reduction); **M** ↓ = Reduced Mobility (% Reduction)

Summary Evaluation:

Radiotherapy Indication: **[ ] yes** **[ ] no**

Tested Joint Score:

Joint Score Value:

Quality of Life Score:

SF-36 Score Value:

Date,
Signature (Physician): ……

Physical Examination / Date ⌊ ⌋⌊ ⌋⌊ ⌋ **(end of RT)** **D**

Involved Joints	**Right Side**					**Left Side**				
Finger (s) No.	**F 1**	**F 2**	**F 3**	**F 4**	**F 5**	**F 5**	**F 4**	**F 3**	**F 2**	**F 1**
DIP / PIP Joint (s)										
MCP Joint (s)										
Wrist										
Elbow										
Shoulder										
Hip Joint										
Knee Joint										
Ankle Joint										
MTP Joint (s)										
DIP / PIP Joint (s)										
Toe (s) No.	**T 1**	**T 2**	**T 3**	**T 4**	**T 5**	**T 5**	**T 4**	**T 3**	**T 2**	**T 1**
Ankylosis										
Swelling / Effusion										
Pressure Pain										
Pain Irradiation										

Tested Functions	**Neutral - Zero - Method**	**Neutral - Zero – Method**
Flexion Extension	**…… / 0° / ……**	**…… / 0° / ……**
Internal Rotation External Rotation	**…… / 0° / ……**	**…… / 0° / ……**
Abduction Adduction	**…… / 0° / ……**	**…… / 0° / ……**
Other Function (s) :	**…… / 0° / ……**	**…… / 0° / ……**
Typical Function (s):		

Legend: **P** = Pressure Pain; **F** ↓ = Reduced Function (% Reduction); **M** ↓ = Reduced Mobility (% Reduction)

Pain: **[ ]** ↓↓↓ (100%) **[ ]** ↓↓ (50 – 99%) **[ ]** ↓ (25 – 49%) **[ ]** no change (± 25%) **[ ]** ↑ deterioration

Function: **[ ]** ↑↑↑ (100%) **[ ]** ↑↑ (50 – 99%) **[ ]** ↑ (25 – 49%) **[ ]** no change (± 25%) **[ ]** ↓ deterioration

Subjective Change: ..... (%) **Objective Change: ..... (%)**

Tested Joint Score: **Quality of Life Score:**

Joint Score Value: **SF-36 Score Value:**

Date,
Signature (Physician): .....

Physical Examination / Date ⌊ ⌋⌊ ⌋⌊ ⌋ (……. months after RT) **E**

Involved Joints	**Right Side**					**Left Side**				
Finger (s) No.	**F 1**	**F 2**	**F 3**	**F 4**	**F 5**	**F 5**	**F 4**	**F 3**	**F 2**	**F 1**
DIP / PIP Joint (s)										
MCP Joint (s)										
Wrist										
Elbow										
Shoulder										
Hip Joint										
Knee Joint										
Ankle Joint										
MTP Joint (s)										
DIP / PIP Joint (s)										
Toe (s) No.	**T 1**	**T 2**	**T 3**	**T 4**	**T 5**	**T 5**	**T 4**	**T 3**	**T 2**	**T 1**
Ankylosis										
Swelling / Effusion										
Pressure Pain										
Pain Irradiation										

Tested Functions	**Neutral - Zero - Method**	**Neutral - Zero – Method**
Flexion Extension	**…… / 0° / ……**	**…… / 0° / ……**
Internal Rotation External Rotation	**…… / 0° / ……**	**…… / 0° / ……**
Abduction Adduction	**…… / 0° / ……**	**…… / 0° / ……**
Other Function (s) :	**…… / 0° / ……**	**…… / 0° / ……**
Typical Function (s):		

Legend: **P** = Pressure Pain; **F** ↓ = Reduced Function (% Reduction); **M** ↓ = Reduced Mobility (% Reduction)

Pain: **[ ]** ↓↓↓ (100%) **[ ]** ↓↓ (50 – 99%) **[ ]** ↓ (25 – 49%) **[ ]** no change (± 25%) **[ ]** ↑ deterioration

Function: **[ ]** ↑↑↑ (100%) **[ ]** ↑↑ (50 – 99%) **[ ]** ↑ (25 – 49%) **[ ]** no change (± 25%) **[ ]** ↓ deterioration

Subjective Change: ..... (%) **Objective Change: ..... (%)**

Tested Joint Score: **Quality of Life Score:**

Joint Score Value: **SF-36 Score Value:**

Date,
Signature (Physician): .....

Radiotherapy in Gorham-Stout Syndrome with Massive Osteolysis of the Cervical Spine

K.Schönekaes – Münster, J. Panke – Paracelsus-Strahlenklinik, Osnabrück, H. M. Gießler – Staedt. Kliniken, Dortmund, Germany

The Gorham-syndrome is known to be a mainly monocentric idiopathic osteolysis mostly occurring in childhood. The first case was published in 1838 by Jackson (6). In 1955 Gorham and Stout described the pathological changes of this disease. (4). The disease is also known as Gorham-Stout-syndrome, as massive osteolysis or as vanishing bone disease. It begins with the exchange of bone with lymphangiomatic tissue. The histological findings are often uncharacteristic and only a replacement of the bone through connective tissue is reported.

Case report

A previously healthy ten year old boy, with no incident of trauma presented with sudden painless and increasing neck stiffness. Neurological examination and all laboratory tests were normal. Initially conventional x-rays showed a single site of osteolysis at the arch of the second cervical vertebra. Later more cervical spine segments were affected. (Fig. 1).

Fig. 1: Conventional radiography of the cervical spine

Within 5 years the whole osteolytic process extended over the upper part of the thorax and onto the base of the skull. The changes at the base of the skull shown in the CT scan were impressing (Fig. 2).

Fig. 2: CT-scan of the base of scull and the upper cervical spine

In MR imaging substitution of the bone marrow signal with a muscle-isodense contrast medium enhanced substrate was seen. (Fig.3).

Fig. 3: MRI of the cervical spine, T1-weighted axial imaging

A biopsy of the second cervical vertebra showed a fibrotic area in the connective tissue with increased vascularization with no indication of malignancy. Over 5 years with a short interruption of the medical results, there was extension of the osteolysitic process from the base of the skull to the upper thoracic spine. 4 years after the commencement of the disease, the patient developed a pericardial effusion in addition to massive persistant chylous pleural effusions. Subjectively he experienced dyspnea, dry cough and angina pectoris as well as increasing sensations of pain in the cervical spinal column. Neurological impairment was not observed. It was impossible to reduce the effusion by medication, and a permanent drainage was necessary. The cervical vertebrae were stabilized with a fixateur.

At this stage radiotherapeutic treatment was initiated. With a linear accelerator and a photon energy of 10 MV a total dose of 36 Gy was applied by a 5 times weekly fractionation with a single dose of 2 Gy per day. The irradiation was performed with two lateral opposing fields in the region of the base of the skull and down to the 6th cervical vertebra (Fig. 4).

Fig. 4: Treatment portals, lateral opposing fields

The irradiation of the upper thoracic region took place with an ap/pa field arrangement. During the therapy the patient experienced minor symptoms of dysphagia, but noticed reduction in the previously mentioned pain. Eventually the pulmonary situation worsened and the patient died pproximately two months after completing the radiotherapeutic treatment.

Discussion

Since defining Gorham Syndrome in 1838, only approximately 200 cases have been reported in the literature. The Gorham syndrome is characterized as a nonhereditary, histologically benign endothelial proliferation of the bone tissue which is accompanied by extensive osteolysis (4).

Histololgically there are angiomatous as well as lymphatic changes and miscellaneous forms described (9). Eventually the involved osseous tissue is replaced completely by fibrotic scar tissue, so that the histological result stays unspecific and the disease should not to be diagnosed without radiological means. The disease is characterised by an increasing osteolytic de-

struction seen in conventional radiological examinations. CT scans are especially suited to detect the osseous changes in the initial phase of the disease. (10). With the MRI the infiltration of the spinal canal and the soft tissue component can be seen. Almost always the disease is limited to one area of the body, whereas limits between different bones are not respected.

The Gorham-syndrome advances localizally. The shoulders and the pelvic bone structures are preferred sites, but all parts of the skeleton can be affected. An involvement of the cervical spine is extremely rare (2). The involvement of the osseous structure of the thorax as demonstrated, however can cause a pleural effusion which may turn out to be fatal event (2). The initial osseous changes do not allow prognostic statements to be made concerning the development and outcome of the disease. Different experiments with various forms of medication are not successful (7, 9). The most important trials concern the irradiation as well as the surgery where necessary with transplantation of osseous structures. When there is involvement of the vertebrae it is also possible to of stabilize the spine with replacement of bone tissue by titane (3).

Cessation of the disease after radiotherapy or resection of the involved area has been described. Although there also are reports concerning reversal of the disease after surgery, resorption of the implanted osseous material can occur as well as after radiotherapy (3. 5. 10).

Conclusion

Because of the rarity of this disease, different treatment regimens have been discussed controversially in the literature (3, 5, 8). The radiotherapy generally leads to rapid pain reduction as well as to a recalcification of the destroyed osseous tissue (1, 5). A total dose of less than 35 to 40 Gy is not recommended (1, 3).

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Literature Commentary:

Is Radiotherapy Useful for Prophylaxis of Restenosis after PTA of the Lower Limb ?

B. Pokrajac, R. Pötter, T. Maca, C. Fellner, , M. Mittlböck, R. Ahmadi, W. Seitz, E. Minar, Vienna:
„Intraarterial Ir192 High-Dose-Rate Brachytherapy for Prophylaxis of Restenosis After Femoropopliteal Percutaneous Transluminal Angioplasty: The Prospective Randomized Vienna-2-Trial Radiotherapy Parameters and Risk Factors Analysis"
Presented at the 41st ASTRO Meeting 1999 and published in
Int J Radiat Oncol Biol Phys 48 (2000): 923-931.

Purpose: The aim of the Vienna-2-trial was to compare the restenosis rate of femoropopliteal arteries after percutaneous transluminal angioplasty (PTA) with or without intraarterial high-dose-rate (HDR) brachytherapy (BT) using an Ir192 source.
Materials and methods: A prospective, randomized trial was conducted from 11/96 to 8/98. A total of 113 patients (63 men, 50 women), with a mean age of 71 years (range, 43-89 years) were included. Inclusion criteria were (1) claudication or critical limb ischemia, (2) de-novo stenosis of 5 cm or more, (3) restenosis after former PTA of any length, and (4) no stent implantation. Patients were randomized after successful PTA for BT vs. no further treatment. A well-balanced patient distribution was achieved for the criteria used for stratification, as there were "de-novo stenosis vs. restenosis after former PTA", "stenosis vs. occlusion", "claudication vs. critical limb ischemia" and above these for "diabetes vs. nondiabetes". PTA length was not well balanced between the treatment arms: a PTA length of 4-10 cm was seen in 19 patients in the PTA alone group and in 11 patients in the PTA + BT group, whereas a PTA length of greater than 10 cm was seen in 35 patients and 42 patients, respectively. A dose of 12 Gy was prescribed in 3-mm distance from the source axis. According to AAPM recommendations, the dose was 6.8 Gy in 5-mm distance (vessel radius + 2 mm). Primary endpoint of the study was femoropopliteal patency after 6 months.
Results: PTA and additional BT were feasible and well tolerated by all 57 patients in this treatment arm. No acute, subacute, and late adverse side effects related to BT were seen after a mean follow-up of 12 month (6-24 months) in 107 patients (PTA n = 54; PTA + BT n = 53). Crude restenosis rate at 6 months was in the PTA arm 54% vs. 28% in the PTA + BT arm (p < 0,013). Actuarial estimate of the patency rate was at 6 months 45% vs. 72% (p < 0,004). Comparison of restenosis rates for the different subgroups with risk factors (restenosis after former PTA, occlusion, and PTA length > 10 cm) showed significant decrease of the restenosis rate, if BT was added. Significant reduction was not achieved in diabetes patients.
Conclusion: BT after femoropopliteal PTA is feasible and a safe therapeutic option. No BT related morbidity was observed. A significant reduction of the restenosis rate was obtained in the PTA + BT arm. Subgroup analysis showed significant decrease of restenosis rate in the subgroups with restenosis after former PTA, occlusion, and PTA length of greater than 10 cm. With dose escalation and reduction of dose variation by a centring device a further significant decrease of restenosis rate can be expected.

Comment:

Percutaneous transluminal angioplasty (PTA), based of the principle of balloon dilatation and recanalization of vessel occlusion or vessel stenosis with intraarterial thrombolysis, is an accepted standard treatment of arterial occlusive disease. The main problems of this method are thrombosis in the early postangioplasty time and restenosis within the first year after dilatation and recanalization, with a frequency of about 30-60%, depending on the report. The restenosis is the subsequent reaction of the vessel wall to a stimulus (for example a catheter manipulation) and to some degree it appears in all cases (5).
Three factors contribute significantly to restenosis after angioplasty: acute elastic recoil, neointimal hyperplasia (cell proliferation after the trauma of dilatation), and negative remodelling (chronic vessel constriction). Different drug treatments with e.g. anticoagulants, antiplatelets and aspirin as well as different technical approaches eg directional atherectomy, rotablation and laser angioplasty have shown little or no beneficial effect in the prevention of restenosis (5, 6).

Preliminary clinical experience and experimental animal studies indicated a significant potential of ionizing radiation in the prophylaxis of restenosis, mostly interpreted as the inhibition of neointimal hyperplasia. The optimal dose amount to 12 to 20 Gy (7).

Prevention of restenosis using intravascular brachytherapy was first introduced and reported for femoropopliteal arteries by the Frankfurt group in the early 1990s. They reported excellent results from a clinical Phase I/II trial for patients with femoropopliteal restenosis after PTA and stent implantation, even after a 6-years follow-up period. A dose of 12 Gy was applied in 3-mm distance from the source axis. A repeated restenosis was occurred only in 3 of 28 patients (1). Furthermore, clinical studies in coronary arteries have underlined the impact of endovascular brachytherapy, leading to a significant reduction of restenosis.

Until relatively recently the use of radiation in this area was not recommended in the standard textbooks (4).

There are a small, but increasing number of controlled clinical trials, which have looked at the value of ionizing radiation in this disorder. Particularly for coronary arteries the impact of intravascular brachytherapy is supported by several recent articles and the FDA approval will be given in the near future (3, 9).
In peripheral arteries there are fewer controlled clinical studies (2, 8).. Therefore the report of Pokrajac et al (6) is an important contribution to this data and it shows that intravascular brachytherapy is equally effective in peripheral vascular diseases.

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Announcements

Archive of Benign Diseases: To achieve and maintain an overview about currently published data, the German Working Group "Radiotherapy for Benign Diseases" and BenigNews will establish an "Archive of Benign Diseases". We would like to ask clinicians any potential authors, who have recently published an article about radiotherapy of benign diseases, to send a reprint to the editorial office of BenigNews. Furthermore, any interested person is encouraged to send a copy of any interesting publication about radiotherapy of benign disease to the editorial office of BenigNews.

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6. *Announcements, advertisements etc.*
   Please contact the publishing office directly on conditions.

Manuscript submission and text preparation (excerpt)
1. Include a diskette or CD-ROM with the text file(s) in Microsoft Word 6.0, 95, 97, or 2000 format and the figures in TIF, BMP, or JPG format. The electronic and printed versions have to be identical.
2. Include an accompanying letter with the signature of the corresponding author and a declaration that he or she is submitting the paper on behalf of all authors and that they have all seen and approved the final version, or, alternatively, with the signatures of all authors stating their approval.

References (excerpt)
1. References in the text should be indicated by numbers in round brackets e.g. (1, 2, 8–9) and all references should be listed at the end of the paper in a separate section and numbered in alphabetical order.

2. *Example of journal citation:*
   Beitler JJ, Smith RV, Brook A, et al.: Benign parotid hypertrophy in HIV+ patients: limited late failures after external radiation. Int J Radiat Oncol Biol Phys 45 (1999) 451–455.
3. *Example of book chapter citation:*
   Notter M: Strahlentherapie bei Pseudotumor orbitae. In: Seegenschmiedt MH, Makoski HB (eds.). Radiotherapie von gutartigen Erkrankungen. Diplodocus-Verlag, Altenberge (2000): pp. 123–136.

"Benign" Calendar of Events

For publication of any relevant events, please notify early enough the **Managing Editor**: Dr. med. Oliver Micke, Westfälische Wilhelms-Universität, Klinik und Poliklinik für Strahlentherapie – Radioonkologie, Albert-Schweitzer-Str. 33, 48129 Münster, Germany, Tel: +49 (0)251 8347839, Fax +49 (0)251 8347355, e-mail: omicke@uni-muenster.de

04.05.-05.05.2001
Interdisciplinary Conference: Radiation Therapy of Benign Diseases
am *Alfried-Krupp-Krankenhaus, Alfried-Krupp-Straße 21, 45117 Essen, Germany.*
Topics: Radiobiological Aspects of Benign Diseases; Individual Radiophysics Planning in Orthovolt Radiotherapy; Orthopedic Clinical Examination of Shoulder, Elbow, Hip and Knee Joints; Radiation Prophylaxis of Heterotopic Ossification; Radiotherapy for Immunological Disorders; Radiotherapy for Organ Transplant Rejection; Stereotactic Radiotherapy of Trigeminal Neuralgia and Focal Epilepsy; Radiotherapy for Benign Parotid Disorders; Free Papers.
Conference Language: German (selected Topics in English)
Contact: Prof. Dr. med. M. Heinrich Seegenschmiedt
Secretariat: Mrs. Astrid Ebel, Mrs. Christiane Kerstan-Sivri,
Klinik f. Radioonkologie, Strahlentherapie & Nuklearmedizin,
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01.09-05.09.2001
European Radiation Research 2001 ERR 2001, 31st Annual Meeting of the European Society for Radiation Biologie (ESRB) and 5. Jahrestagung der Gesellschaft für Biologische Strahlenforschung (GBS)
in *Dresden, Germany*
Contact: Priv.-Doz. Dr. med. W. Dörr, Klinik und Poliklinik für Strahlentherapie und Radioonkologie, Medizinische Fakultät Carl Gustav Carus,
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E-mail: doerr@rcs.urz.tu-dresden.de

8.09-11.09.2001
7. Jahreskongress der Deutschen Gesellschaft für Radioonkologie (DEGRO2001)
in *Hamburg, Germany.*
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Abteilung für Strahlentherapie und Radioonkologie
Klinik und Poliklinik für Radiologie, Universitätsklinikum Hamburg-Eppendorf
Internet: http://www.degro.org

04.11-08.11.2001
43rd Annual Meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO 2001)
In *San Francisco, CA, USA*
Contact: Internet: http://www.astro.org

17.11.2001
3rd Münster Workshop on Trace Elements and Electrolytes in Radiation Oncology & 4. Scientific Meeting of the German Working Group Trace Elements and Electrolytes in Radiation Oncology (AKTE)
in *Münster, Germany*
Contact: Dr. O. Micke, Klinik und Poliklinik für Strahlentherapie – Radioonkologie, Westfälische Wilhelms-Universität, Albert-Schweitzer-Str. 33, 48129 Münster, Tel: +49(0) 251 83-47839 or -47831, Fax. –47355,
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IMPRESSUM

BenigNews
Founded 2000

Aims and Scope
BenigNews is the official information letter of the German Working Group "**Radiotherapy for Benign Diseases**" and all cooperating international groups. BenigNews intends to improve the information and communication about all fields of radiotherapy for non-malignant or benign diseases including basic research in biology, physics and technical applications and clinical research. The official language of the letter is English. Help will be provided for translation of articles written in other than English language.

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