German Cooperative Group

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

Radiotherapy for Benign Diseases

Inside this Issue:

Editor's Corner

Dear Colleagues and Friends of Radiation Medicine,

we are pleased to present you the second edition of **BenigN**[ews] in 2001 which contains as a main topic "painful heel conditions". It is rather symbolic that we are keep on to walk with BenigNews through several other interesting topics. We start out with an overview on diagnostic procedures for painful plantar and dorsal heel conditions; we continue with a clinical paper on radiotherapy for painful heel spur and present a detailed scoring system and documentation format for the clinical users. This scoring system has been developed in a multi-center approach by the German Cooperative Group on Radiotherapy for Benign Diseases. It will be used for a large prospective study which is currently in progress and compares pain medication versus different radiation dose concepts.

This issue also contains an interesting paper on radiotherapy for vertebral hemangiomas. In addition, we introduce a rare syndrome with a case report of a patient suffering from a Kasabach-Merrit-Syndrom. In future issues of BenigNews further rare case reports will be presented together with a short literature review.

We continue the commentary section of BenigNews with a discussion on the treatment of Peyronie's Disease (IPP = Induratio Penis Plastica) using a fractionated radiotherapy concept. This paper should encourage us to perform a patterns of care study (PCS) on this topic in Germany and get in touch with our referring urologists.

We also report on a scientific award, the Paul-Krause-Prize, which has been recently awarded to Dr. Ulrich Schäfer (University of Münster, Germany) for his experimental radiobiological thesis on intravascular radiotherapy paper.

Finally, we publish the Meeting Abstracts of the Essen Symposium on "Radiotherapy for Benign Diseases; the conference was held on May 4 – 5, 2001. The next conference will take place on May 3 – 4, 2002 in Essen. The preliminary program outline is published in this issue.

Again, for the next **BenigN**[ews] we would appreciate further conversation, comments and suggestions from all readers of the upcoming issues via phone, fax, internet or personal communication.

With best regards,

M. Heinrich Seegenschmiedt, Essen (Germany)
& Hans-Bruno Makoski, Duisburg (Germany)

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Radiotherapy of the Painful Plantar Heel Spur

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Summary
Aim: In a retrospective analysis the efficacy of radiotherapy of painful calcaneal spur was evaluated for an individual dose concept.
Patients and methods: From 1989 to 1997 141 evaluable patients (58 male, 83 female) with a mean age of 55 (22 – 82) years received orthovoltage radiotherapy (175 kV, 20 mA, SSD 40 cm) with an individual dose concept. First a series of 6 x 1 Gy within 2 weeks was applied. After an interval of 10 to 12 weeks the efficacy checked up. In case of persistent pain the patients received a second series in the same modality. Total 161 heels (right 84; left 77; both sides 20 of it) were treated. The mean duration of pain symptoms before start of therapy was 9 months. 37 % of the heels were previously untreated. 24 heels (15%) received 2 series of radiotherapy.
Results: A positive effect of radiotherapy we observed in 89 % of treated heels with a complete pain relief in 63 % within 6 weeks on average after completion of treatment. A clear improvement of pain was reached in 20 % and a minor relief of pain in 6 %. The rate of pain relapse was 19 % at a mean follow up of 30 months (1 to 103 months).
Conclusion: Our results prove the high efficacy of radiotherapy of painful heel spur. A total dose of 6 Gy seems to be sufficient in most of the cases. A second series of radiotherapy should be applied in case of persistent pain.

Radiotherapy of painful calcaneal spur is considered as a very effective treatment method. But there is no clear idea about the optimal dosage and fractionation and the role of high voltage radiotherapy. As a basic for further research the efficacy of orthovoltage radiotherapy was evaluated in a retrospective analysis for an individual dose concept used in our hospital for the last ten years.

Patients and methods

From January 1989 to December 1997 total 235 heels were treated in the Department of Radiotherapy, Zentralklinikum Suhl because of painful plantar heel spur with an individual dose concept. 141 patients (58 male : 83 female = 1 : 1,43) were evaluable for assessment of effect and follow up. The mean age of the 141 patients was 55 years with a range from 22 to 82 years (Figure 1).

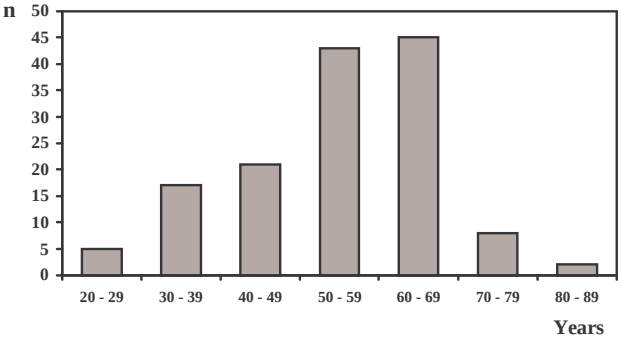

Fig. 1: Age distribution of 141 patients treated with radiotherapy for calcaneal heel spur

Total 161 heels (right side 84; left side 77) were evaluable for this analysis. In 20 patients radiotherapy was administered for both sides. The mean duration of pain symptoms before start of therapy was 9 months (1 – 120 months). 28 of the heels (17 %) had an anamnesis of pain for more than 12 months. 60 heels (37 %) were previously untreated. The other 101 heels obtained 1 or more treatment options without respectively without full success preferring insole support (n = 63), local injections (n = 45), ultrasound therapy (n = 38) and others (n = 38).
Radiotherapy was administered with an orthovoltage therapy unit with 175 kV, 20 mA, 0,5 mm copper filtering and a source-skin-distance of 40 cm. The field of a size 6 x 8 cm was focused from plantar on the heel. First a series of 6 x 1 Gy within 2 weeks was administered. After an interval of 10 to 12 weeks the efficacy of the treatment checked up. In case of persistent pain the patient received a second series in the same modality. 24 heels (15 %) received 2 series of radiotherapy.
The assessment of the effect of radiotherapy was done by a study of medical records and interviews of the patients immediately at the end of therapy, 10 – 12 weeks after completion of first series and final after completion of second series. Four categories were formed for assessment of effect according to von PANNEWITZ (1): 1.Complete pain relief; 2.Clear improvement (only occasional pain); 3.Minor improvement (pain persists with improvement, pain is tolerable); 4.No change (only temporary improvement, no change respectively worsening of pain). Moreover a long-time follow up was performed to seize the cases of pain relapse.

Results

In 29 heels (18 %) we observed a clear acute pain enhancement during the therapy. Immediately at the end of first series of radiation treatment only 4 % (6 heels) achieved a complete pain relief, while 50 % (80 heels) perceived no change or worsening of pain quality. After 3 months already 56 % (91 heels) showed complete pain relief and after completion of the treatment with a second series in 24 heels 63 % (101 heels) were free of pain. A clear improvement was observed in 20 % (32 heels) and a minor improvement in 6 % (10 heels). Only 11 % (18 heels) did not react to radiotherapy (Figure 2).

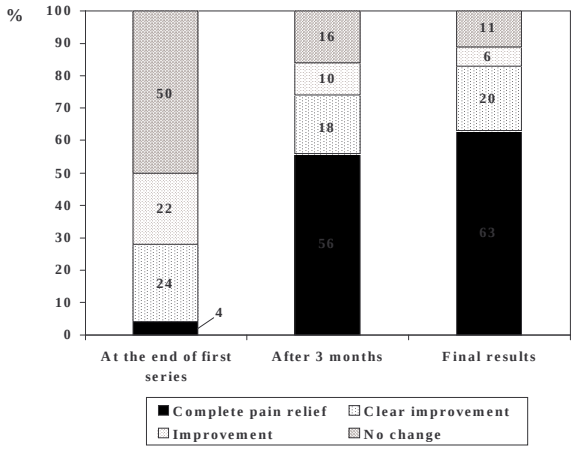

Fig. 2: Effect of radiotherapy for calcaneal heel spur

The time to success of radiotherapy after completion of treatment was 6 weeks on average. Most of the patients perceived the positive effect within 12 weeks. Only in 9 of 143 successful treated heels (6 %) it takes more than 12 weeks to reach the analgesic effect.
The heels previously untreated better responded to radiotherapy (72 % complete pain relief) than those unsuccessfully treated before with another therapy (58 % complete pain relief). Heels with an anamnesis of pain more than 12 months did also react worse to radiation treatment (only 32 % complete relief of pain). Older patients (age >= 50 years) showed a better response (70 % complete relief) than younger below 50 years (46 % complete relief).
The global rate of pain relapse was 19 % (27/143 successful treated heels) at a mean follow up of 30 months (1 to 103

months). Described as a hazard function the probability of relapse was 7 % at 1 year, 15 % at 2 years, 21 % at 3 years and 32 % at 5 years after completion of treatment.

Discussion

In this place We will not discuss the clinical feature of calcaneodynia or basic research. We like to refer to the fundamental publication of clinical data (2) and the basic publications of experimental research (3-5).

Our results verify the good effect of low-dose radiotherapy in the treatment of painful calcaneal spur with an orthovoltage therapy unit. Most of publications in former times used also orthovoltage radiation therapy with good overall results (2,6-11). But frequently there was no clear information about single and total doses and the fractionation respectively it was specified only a range of single and/or total doses (6-8,10). In recent time 1.more studies with a major number of patients and an uniform dose concept (2, 11-13), 2.studies using high voltage radiotherapy (12-14) and 3.studies with use of individual scores (2, 13) were published (Table 1).

In our retrospective study we pursued the goal of verification of the effect of radiotherapy with an usual dose concept in our hospital with a large number of uniform treated heels. Under the condition of a retrospective analysis it was not possible to use individual scores for assessment of effect. Nevertheless the results confirm that our dose concept is useful to treat painful heel spur. In univariate analysis of predictive factors of success of the treatment with regard to the criterion "complete pain relief" there was statistical significance (Chi-square-test) for better outcome for patients with short pain anamnesis (<= 12 months vs. > 12 months, $p < 0,001$) in agreement with other authors (2,15) and for older patients (<50 years vs. >= 50 years, $p < 0,01$). This is a new point of view we didn't found described in the literature. Although patients without unsuccessful pretreatment react better to radiotherapy the difference between the groups don't reach significance ($p = 0,07$). No difference was observed referred to gender (male vs. female, $p=0,78$) and site of disease (right vs. left, $p = 0,82$).

Conclusion

Our results prove the high efficacy of radiotherapy of painful heel spur. A total dose of 6 Gy seems to be sufficient in most of the cases. At an interval of 12 weeks a second series should be applied in case of persistent pain. The meaning of predictive factors and dosage is furthermore not clear. In future randomized studies to find out the optimal dosage of radiotherapy it is necessary to pay attention to possible predictive factors like age of the patients at start of therapy.

Reference	Patients	Heels	Dose (Gy)	Type of RT	Response Rate (%)	CR (%)	PR (%)	NC (%)
Mitrov & Harbov (1967) (6)	1520	1520	0,5 – 1,5 / 3,0 – 6,0	OV	88	50	38	12
Zschache (1972) (7)	49	49	0,75 – 1,5 / 2,25 – 4,5	OV	86	12	74	14
Mantell (1978) (9)	17	26	2,0 /10,0	240-300 kV	65	53	12	35
Basche et al.(1980) (8)	102	102	0,3 – 0,5 / 4,0	120 kV	90	32	58	10
Schäfer et al. (1995) (14)	18	21	0,5 – 1,0 / 2,0 – 4,0	HV	67	58	8	33
Seegenschmiedt et al. (1996) (2)	141	72	1,0 / 12,0	250 kV	100	67	33	0
		98	0,3 – 0,5 / 3,0 – 5,0	200 kV	95	72	23	5
Oehler & Hentschel (2000) (10)	212	258		OV	88	81	7	12
Koeppen et al. (2000) (11)	673	673	0,3 / 1,5 – 3,0	250 kV	78	13	65	22
Scheiber et al. (2000) (12)	70	87	1,0 / 6,0	6 MV	86	67	29	14
Heyd et al.(2001) (13)	105	127	1,0 / 6,0 – 12,0	6 MV	88	46	42	12
Glatzel et al. (2001)	141	161	1,0 / 6,0 – 12,0	175 kV	89	63	26	11

Table 1: Results of radiotherapy of painful heel spur (Overview of literature), RT = Radiotherapy, OV = Orthovoltage radiotherapy, HV = High voltage radiotherapy

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Radiotherapy of Vertebral Hemangiomas

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Summary
Two cases with symptomatic vertebral hemangiomas underwent conventional fractionated radiotherapy (RT) with a total dose of 30 Gy as the primary method of treatment and post-surgical treatment for the prevention of a local recurrence. After a follow-up period of nine months, complete symptom relief occurred in both of the cases. In order to minimize the risk of radiation-induced neoplasms and to avoid early toxicity we conclude that the total doses for the management of vertebral should not exceed 30 Gy.

Hemangioma is a benign neoplasm which is composed of blood vessels (5, 23). In the skeleton, the sites most commonly affected are the skull, the spine, the sternum and the metaphyses of the long tubular bones (6, 24). Autopsy studies revealed an incidence of vertebral hemangiomas (VH) in the range 10-12% (15, 26). Most of the cases are detected as incidentally lesions (8, 23, 24) and only 0.9-1.2% develop clinically relevant symptoms (23). The age distribution peaks between the 3rd and 5th decades with a predominance in females (5, 10, 17, 23-25). Predilicted locations are the dorsal spine and the upper lumbar spine (4, 5, 6, 8, 10, 15, 17, 23-27).
Their pathogenetic origin is suggested in a congenital loss of differentiation of embryogenic vessels or embryonal cell rests which are trapped into the vertebral body (10, 12, 19, 24). Hemangiomas are harmatoms, and by definition, they do not expand by a mitotic activity (10, 12). Therefore, hemorrhage and thrombosis, organization and recanalization, and furthermore, a hemodynamic stress or decrease of the supporting stroma has been suggested as possible reasons for the release of the symptoms (8, 12, 24). They can mimic the symptomatology of all other types of spinals tumors (9, 17) and in approximately 55% they are only associated with painful symptoms and in 45% they cause a variety of neurological deficits ranging from nerve root compression to severe compression of spinal cord resulting in a transverse lesion of the spinal cord (23). The morphological findings include a stretching of the periosteum of the vertebral body, an intraspinal expansion, an expansion into the extradural space, pathological fractures and also ischemia of the myelon (1, 9). During pregnancy a release of the symptoms is possible by a compression of the Vena cava inferior and the increase of the blood volume up to 30-50% (18, 19, 25). For the lacking evidence of estrogen receptors (25) a direct influence on the endothelium cell linings seems to be improbable and the release of the symptoms is triggered by hemodynamic factors.

Only the symptomatic vertebral hemangiomas (sVH) cause the necessity of treatment and the use of surgical procedures, such as decompressive laminectomy (1, 8, 9, 10, 12, 17, 19, 21), vertebraectomy (8) or ligation of segmental arteries (3) has been reported. Conservative methods include embolizations (8, 12, 20), vertebroplasties (14), alcohol injections (4) and also RT (1, 3, 6, 8, 10, 12, 13, 17, 19, 21, 23, 24, 27) used as single modalities or in combinations. We present two cases who underwent RT as the primary or postsurgical method of treatment and discuss the indication and the possibility of radiation risks.

Case reports

Case 1

A 72-year old female complained of progressive back pain in the lower lumbar spine and both sides of the dorsal chest wall which had occurred within two weeks. On examination, the only finding was percussion pain upon the lower thoracic spine and there was no evidence of a transverse lesion of the spinal cord. Plain radiographs of the thoracic spine produced evidence of a depreciation of the T8 vertebra due to a pathological fracture. Additional CT scans revealed the typical polka-dot-aspect of a vertebral hemangioma (Fig 1).

Fig. 1 CT scan of the T8 vertebra demonstrating areas of an increased enhancement corresponding to the hyperplastic trabecular architecture laying between ectatic blood vessels (polka-dot appearance). An intraspinal expansion was not detected.

The patient was immobilized and because of the age and a history of cardiovascular disease she was considered for a primary radiotherapy. After localization of the treatment portal including T7-T9 vertebrae we applied with single field irradiation (SSD = 100 cm) a total dose of 30 Gy given in five weekly fractionations of 2 Gy using 6 MV photons from a linear accelerator.
During the course of RT we did not observe any early toxicity and in first follow-up examination at six weeks after the treatment the patient was completely mobile and had a marked relief of the painful symptoms. Nine months after the treatment she had a complete relief of pain and a MRI of the spine demonstrated a moderate fatty change as a sign of osteoporosis and a slight narrowing of the spinal canal at the T8 vertebra due to the compression fracture. Stenosis of the spinal canal, signs of a myelopathy or a paravertebral mass lesions were not detected. In the whole spine was no evidence of any active vascular malformation.

Case 2

A 47-year old female developed pain in the upper thoracic spine and a progressive weakness and numbness of both legs associated with a progressive inability to walk. When examined, the findings include percussion pain upon the upper thoracic spine, sensory abnormalities descending from the nerve root T5 and a symmetrical hip-flexion weakness of strength grade 4-5 with no disturbance of the reflex activity of the lower extremities.
A MRI of the spine showed an increase of signal intensity in the T3 vertebra and an intraspinal mass lesion causing severe compression of the spinal cord (Fig. 2).
Because of the initial transverse lesion a laminectomy was performed. Intraoperatively, a gray vitreous tumor of a flabby consistence was found invading into the spinal canal from dorsal part of vertebral body and histological examination produced evidence of a cavernous bony hemangioma. Postoperatively, the patient recovered soon and a marked symptom

relief occurred within a few days. A MRI study on the third post-operative day showed a marked reduction of the tumor mass. An intraspinal tumor was not detected but the T2-weighted sequence demonstrated an increased signal due to residual tumor in the area of the left pedicle.

Fig. 2: T2 weighted sequence of an MRI of the spine which demonstrates a severe increase of the signal intensity in the dorsal part of the T3 vertebra. The lesion mass invades the spinal canal and has led to a myelon compression from the posterior aspect.

Therefore a post-surgical RT was applied using the same dose fractionation schedule and radiation technique as in case report 1. Adverse effects were not noted and at the end of the outpatient care the patient was completely mobile and neurological examination disclosed a residual numbness descending from nerve root T8 and slight disturbance of motor coordination of the lower extremities. At six weeks after RT the clinical findings were unchanged. At nine months follow-up after the combined treatment the patient was free of symptoms. A MRI of the spine showed a decrease of the signal intensity in the left pedicle of T3 vertebra.

Discussion

The management of symptomatic vertebral hemangiomas depends on the severity of the symptomatology, and may be either conservative or surgical. In clinical practice it has been proven as convenient to divide four categories of cases (Table 1) (9, 17).

Classification	Clinical signs
Group I	Compression of the spinal cord causing a transverse lesion
Group II	Compression of spinal cord without evidence of a transverse lesion
Group III	No compression of spinal cord but evidence of local symptoms
Group IV	No evidence of clinically relevant symptoms

Table 1 Clinical classification of symptomatic vertebral hemangiomas

Whereas *group IV* did not cause the necessity of treatment, in *group II* and *group III* there exists a relative indication of treatment using the different modalities as a single method or in combinations. Because of the delayed effects of RT (4) there exists for group I an indication for an immediate surgical decompression in order to avoid a persistent myelopathy (8). The rational basis for the indication of a post-surgical RT (Case report 2) are relapsing symptoms in up to 30% of cases with a follow-up period > 3 years. 90% out of these cases developed a local recurrence within two years after surgery (21). The use of primary RT should be reserved for cases with contraindications for a surgical procedure (Case report 1) or multifocal disease.

Radiation target is the endothelial cell (11) and an impairment of circulation and vascular damage which eliminate abnormal veins and capillaries has been suggested as possible mechanisms of RT (6, 10). Usually hemangiomas does not reduce the stability of the vertebral body because of the compensatory hypertrophy of the trabecular architecture (10) and pathological fractures (Case report 1) occurs only in cases with severe involvement of the vertebral body. A radiologically detectable resclerosis is commonly not observed after RT (6, 10). The relief of painful symptoms and neurological deficits which occurs from a few months up to two years after RT should be the end-points of the evaluation of treatment outcome (10).

Since the first report by Bailey and Bucy (1) the efficacy of RT in the treatment of vertebral hemangiomas has been described in numerous reports (1, 3, 6, 8, 10, 12, 13, 17, 21, 23, 24, 27). The largest series of 66 sites in 62 patients was collected between 1939-1975 by Glanzmann et al (10) in which occurred a staple decrease of symptoms in 60% of cases. Currently, a literature review on 210 cases from 55 other reports between 1929-2000 which were treated with RT alone or in combination with other methods demonstrated that in 54% occurred a complete relief, in 32% of partial relief and only 14% were not improved (13). An analysis of 63 cases from 21 reports in which RT was used as the sole method of treatment showed that 57% had a complete relief, 32% a partial relief and 11% were non-responders (13). This literature analysis confirmed the results of Krueger et al (17) who demonstrated also no significant differences in the number of patients achieving full recovery after surgery followed by RT (61%) (43/70) and RT alone (59%) (26/44).

Currently total doses of 30-40 Gy are recommended for a sufficient local control (6, 8, 10, 24, 25, 27). In the series by Fox and Onofrio (8) a total dose of 10 Gy has been proven ineffective. With regard on our own results and the experimental data by Handl-Zeller et al (11) we believe that a total dose of 30 Gy given in five weekly fractions of 2 Gy is sufficient and carries a minimal risk of tumor induction and of early toxicity related to use of RT.

Yang et al (27) reported on ulcerations of the skin within 10 months after administration of orthovoltage x-rays with a total air dose of 8,000 R (skin dose about 11,000 R) and telecobalt irradiation with 70 Gy. Furthermore, literature reviews has demonstrated that only total doses >30 Gy are associated with an increased risk of radiation-induced sarcomas of bone and soft tissue (2, 16). Concerning RT of angiomatous lesions of bone a tumor induction and malignant transformation has been reported within 2-17 years after repetitive irradiation with 2x40 Gy and 2 x 27,5 Gy (7, 22). In order to avoid repetitive irradiation, pre-operative embolization is the method of choice for the prophylaxis of intraoperative bleeding (20) and the use of RT should be reserved for the sterilization of post-surgical residual tumor in order to prevent the local relapse of symptoms.

Conclusions

RT is an effective a safe method for the management of symptomatic vertebral hemangiomas. Typical indications are the post-surgical RT for the prevention of local recurrences and the primary irradiation in cases with contraindications for a surgical procedure. The current recommendations for the dose-fractionation schedules are not associated with an early or late toxicity. In order to minimize the risk of radiation-induced soft tissue and bone sarcomas the total doses should not exceed 30 Gy.

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German Cooperative Group (GCG) on RT for Benign Diseases

Calcaneodynia - Score

Patient ***Date of Birth***

....

Address

.....

Plantar Heel Spur **Dorsal** Heel Spur **Achillodynia**

Pain **only** right (R) **only** left (L) **R** > **L** **R** < **L** **R** = **L**

- **Direction** **no** direction **to the** sole **and** forefoot **in the** calf lower leg **both** directions
- **Onset** **creeping** / **chronic** **acute / sudden** **not to explain**
- **Time / Type** **onset of strain** **permanent at daytime** **at rest** **at night**

Grade: ....

- **Release** **w/o** strain while **standing** while **walking** while **jumping**

Grade: ....

- **Additional complaints:** .....

Effects on Profession / Sports only **profession** only **sports** **both**

Practiced **Profession** : .....

able to work **unable** to work **no profession** before treatment

Practiced **Sport** : .....

fully able to practice **restricted** practice **not able to practice**

Pretreatment (Please mark appropriate fields !) **from** ..... / ..... **to** ..... / .....

	Physical Measures		**Orthopedic Measures**
	Cold / Heat Applications		External Stabilization Aid
	Ultrasound / Lithotrypsy		Shoe Inlays / Insoles
	Microwaves / Electric Currents		Other Cushion / Padding
	Medication / Injections		**Surgical Measures**
	Oral Meds. :		Which:
	Injections :		

Functional Tests Toe Stand Toe Walking Heel Stand Heel Walking

(✓ = possible)

German Cooperative Group (GCG) on RT for Benign Diseases

Calcaneodynia - Score

Applicable for the following disease entities: **Plantar Heel Spur** / **Achillodynia**

Evaluation: **before RT** ; **during RT** ; Weeks / Months / Years **after RT**

Criteria	Extent of Symptoms / Alteration	Points
1. Pain Symptoms	S = Pain at **Strain**	6 / 4 / 2 / 0
	N = Pain during **Night Time**	6 / 4 / 2 / 0
(total: 30%)	D = Pain during **Day Time** (continuously)	6 / 4 / 2 / 0
	R = Pain at **Rest** (following any kind of strain)	6 / 4 / 2 / 0
	I = Pain at **Initiation of Movement** / Morning Stiffness	6 / 4 / 2 / 0
per single criterion:	none = 6 ; slight = 4 ; moderate = 2 ; severe = 0 points ⇨	
2. Use of Appliances	None	15
	Orthopedic shoe, Insoles, heel cushion	10
	One cane or crutch	5
(total: 15%)	Two canes or crutches	0
	⇨	
3. Professional Activities	No limitation, maximum professional strain possible	20
	Slight limitation, normal professional work possible	10
	Moderate limitation, reduced professional activity	5
(total: 20%)	Severe limitation, daily professional work impossible	0
	⇨	
4. Daily / Leisure Activities	No limitation of daily and leisure activities and sports	15
	Slightly limitation / reduced leisure activities and sports	10
	Moderate limitation / no leisure activities and sports	5
(total: 15%)	Complete limitation of any daily and leisure activities	0
	⇨	
5. Gait / Limp	No limp, normal walking is possible without a limitation	20
	Slightly altered, limp after walking **> 1 km (2 blocks)**	10
	Moderately altered, limp after walking < **1 km (2 blocks)**	5
(total: 20%)	Severely altered, normal walking is impossible	0
	⇨	
Total Score	**Sum of the single scores 1 + 2 + 3 + 4 + 5** ⇨	

modified from: Heyd et al.: Radiology (2001) and Seegenschmiedt et al.: Radiology (1996)

Subjective estimation of the overall quality of life by the individual (X) :

☹☹ ☹ 😐 ☺ ☺☺

[---------i---------i---------i---------i---------I---------i---------i---------i---------i---------]

Date **Physician – Signature**

Kasabach - Merritt Syndrome: Case Report and Review of Therapeutic Options

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Kasabach-Merritt syndrome (KMS) is defined by a huge hemangioma with thrombocytopenia and consumption coagulopathy (1) due to endothelial defects within the hemangiomas causing platelet activation, platelet-fibrin thrombosis formation, consumption of clotting and coagulation factors and increased fibrinolysis (2-5). Almost 200 cases have been reported in the literature since Kasabach and Merritt published the first case in 1940. More than 80% of the cases occur within the 1st year of life (6).

Various treatment regimes have been published with inconsistent results. There are two major treatment objectives – control of the coagulopathy and thrombocytopenia and eradication of the hemangioma. Consequently, different treatment regimes are performed, including systemic corticosteroids (7, 8), irradiation (9-13), compression (14), embolization (15, 16), antifibrinolytic agents (5, 17), platelet aggregation inhibitors (18), interferon (19-21), and other strategies (22-24). Hemangiomas in childhood have been successfully treated with radiotherapy. In recent years this practice has been abandoned for a number of reasons. First, some of these lesions regress spontaneously and require no therapy. Second, radiotherapy can disrupt the growth pattern of the irradiated tissue and cause structural anomalies in pediatric patients. Third, irradiation is associated with a small but definite risk of inducing malignancies. However, in certain situations, e.g. after failure of corticosteroid treatment, radiation therapy is indicated (25).
This report describes a male neonate with Kasabach-Merrit syndrome involving the upper right cervical region for whom radiation therapy combined with interferon alpha was beneficial after failure of corticosteroids.

Case report
A male neonate, born 13.2.99 following an uneventful pregnancy and delivery, was referred to the Department of Pediatrics of the University of Muenster, Germany for management of a large mass in the right upper cervical region. The tumor had been present at birth and had subsequently enlarged.
Sonography revealed a mass of 2x2x3 cm at 4 days of age, which had increased to 3x3x3,5 cm three weeks later.
A hemangioma (5,5x3,5 cm axial) was diagnosed by MRI at 6 weeks of age extending from the right basilar cranium to the deep cervical area with contact to the A. carotis interna. Nuchal muscles were infiltrated. The hemangioma extended to the dura mater at C1/C2 and encased the right A. vertebralis (Fig. 1a).

Fig. 1a: Coronal MRI scan showing the large hemangioma in the cervical region prior treatment.

Platelet counts were decreased to 47.000/ml (normal: 150.000-450.000/ml), prothrombin time (Quick) was normal (93%; normal: > 70%), activated partial thromboplastin time (APTT) was slightly increased (45,5 seconds; normal: < 36 sec.). Fibrinogen was low with 41 mg/dl (normal: 180-450 mg/dl) and fibrin degradation products (FDP; D-dimers) were 2 mg/ml (normal: < 2 mg/ml). Two days later, platelet counts were 16.000/ml, prothrombin time was 91%, and APTT was 45 sec. Fibrinogen was 37 mg/dl and D-dimers were 8 mg/ml. A consumption coagulopathy was diagnosed. Oral prednisolone therapy (5 mg/kg/day) and heparin therapy (300 U/kg/day) were started at 41 days of age. No therapeutic effect was observed. Two weeks after the beginning of the prednisolone therapy, laboratory data were as follows; Platelet count 10.000/ml, prothrombin time < 20%, APTT > 200 sec., fibrinogen < 20 mg/dl and D-dimers 4 mg/ml, indicating disseminated intravascular coagulation (DIC).

Fig. 1b: Coronal MRI scan post-treatment.

Due to tumor progression and DIC, emergency radiation therapy was performed using electron beam therapy (14 MeV) at a single dose of 1,5 Gy (field size: 10x10 cm). Two days later, the hemangioma had enlarged further (7,5x7x5 cm) and an inspiratory stridor had developed. Irradiation was continued by 60Co g-ray (field size: 7,5x10 cm) with 2 Gy per day until a total dose of 9,5 Gy (Fig. 2a).

Fig. 2a: The hemangioma at the last day of the radiationtherapy with erythema

Prednisolone therapy was slowly decreased. At the fifth day of radiotherapy, the laboratory data had improved (platelet count 28.000/ml, prothrombin time 90%, APTT > 200 sec., fibrinogen < 40 mg/dl, D-dimers 4 mg/ml) (Fig. 3). Following irradiation, subcutaneous interferon alpha therapy was performed for six weeks with gradually increasing doses up to 3 million U/m2/day. Platelet counts increased to normal, the tumour regressed during the 8 weeks following irradiation treatment (Fig. 1b). 6 weeks later, laboratory data were nearly normal (platelet count 200.000/ml, prothrombin time > 100%, APTT 38,7 sec., fibrinogen 204 mg/dl, D-dimers 4 mg/ml) (Fig. 3).

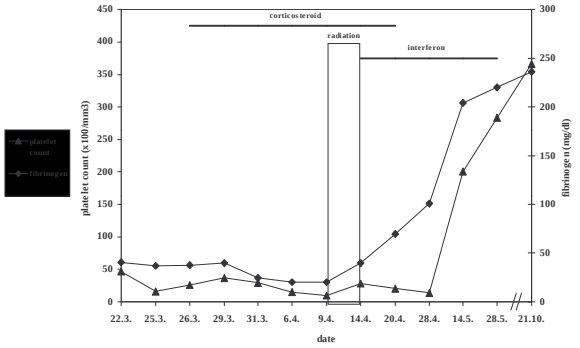

Fig. 3: Platelet levels (▲) and fibrinogen levels (◆) in relation to treatment.

An MRI control one month later showed a decrease of the tumor volume to 3x3x4 cm, no contact to the dura mater and no compression of the larynx or the pharynx. 6 months after therapy, plate-let counts and coagulation profile were still normal and the tumor was hardly visible (Fig. 2b). Until now, no severe acute side effects have been observed.

Fig. 2b: The hemangioma 6 months after the end of radiotherapy.

Discussion

The management of KMS has been widely discussed in previous reports. Steroid therapy plays a major role in the current treatment of childhood hemangiomas. Fost and Easterly (26) were the first to report a dramatic response of cavernous hemangiomas to oral prednisone. Many authors have since confirmed that 2-5 mg/day of prednisone induces regression of hemangiomas after 2-3 weeks. In contrast to the excellent steroid response rate for skin hemangiomas (90%) a similar result has not been reported for Kasabach-Merritt syndrome (30-50%) (10, 27). It has been concluded that in patients not responding to corticosteroids alternative therapies (e.g. radiotherapy and/or interferon alpha) should be used within 3-4 weeks (28). Indications for interferon alpha therapy include hemangiomas that are cosmetically or functionally deforming, of massive size, or life-threatening (29-32). The current literature suggests a minimum response rate to interferon alpha therapy of 60% with limited reversible side effects (20, 33). Adverse effects of interferon alpha include constitutional symptoms e.g. fever, malaise, and fatigue, elevated liver enzymes, nausea, renal failure, transient neutropenia and anemia, hypothyroidism, bone marrow suppression, myalgia, and especially neurological symptoms e.g. gait abnormalities, memory disturbances, ataxia, paresthesia, numbness, oculomotor nerve paralysis, retinopathy, spastic diplegia (34, 35). Nevertheless, treatment with interferon alpha should - like radiotherapy - only be considered for life-threatening hemangiomas that are unresponsive to corticosteroids.

In Kasabach and Merritt`s original report 60 years ago, the treatment modality used was radiation therapy (1). Initially, radiotherapy was the most popular method to treat hemangiomas. Hemangiomas were considered to be very radiosensitive, especially when treated early. Approximately 85% of hemangiomas treated with radiotherapy prior to 1960 completely resolved and 15% showed improvement. Occasionally hemangiomas were resistant to radiotherapy. 6-15% of the patients had scarring of the skin, skin atrophy, increased pigmentation or telangiectasis. Many children treated for skin hemangiomas prior to 1960 have now reached adulthood, and additional late effects have been reported such as breast hypoplasia, growth retardation and radiation-induced malignancies. Treatment side effects were related to total dose and treatment volume as well as to inadequate radiotherapy technique.

It is important to recognize the risks involved in using ionizing radiation to treat a benign, potentially life-threatening disease. A retrospective study of 18.000 patients treated with radiotherapy for hemangiomas in childhood found a significantly increased dose dependent risk of breast cancer, brain tumors, papillary thyroid cancer and bone tumors. Furst reported a cancer incidence in 234 (1,53%) of 15.336 patients with hemangioma who received radiotherapy and in 34 (1,26%) of 2.694 patients with hemangioma who received no radiation (36, 37). This difference was not significant.

We conclude that radiotherapy in view of these severe long-term sequelae is no longer an appropriate treatment for skin hemangiomas without severe life-threatening coagulopathy. A 2-3 week course of oral prednisone is the initial treatment of choice. Complicated cavernous lesions can be an indication for radiotherapy when alternative therapies e.g. corticosteroids have failed. A retrospective analysis of 153 reported cases of KMS sup-ports this conclusion (2). With the combination of radiation and steroids mortality rates were 2,5% compared to 30% in patients receiving no treatment. Other treatment modalities did not appear to be as beneficial. In the literature, the response to radiotherapy was reported in 60% to 100% (11, 36, 38, 39). It must be stressed that in a life-threatening condition, emergency radiation therapy should be considered as the first choice of treatment and should not be delayed if rapid steroid response is not forthcoming. When radiotherapy is used, the lowest dose should be used, so that the incidence of possible late effects and secondary malignancies is reduced. Cavernous hemangiomas with thrombocytopenia generally will respond to total radiotherapy doses of 7 Gy to 20 Gy (40), though in some cases a dose of 10 Gy by conventional fractionation seems to be sufficient (13). In this case, a dose of 9,5 Gy was necessary for the control of symptoms.

Conclusion

Radiotherapy and interferon alpha are used in children with life-threatening hemangiomas. In this case of KMS, radiotherapy controlled disseminated intravascular coagulation and improved the coagulation profile. It is difficult to determine if the documented response was due to radiotherapy, interferon alpha or both treatment regimes. We conclude that radiotherapy, despite possible severe sequealae in some cases, is still indicated in the treatment of childhood hemangioma if the clinical case is complicated and alternative therapies have failed.

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Imaging in Benign Diseases:

On the Diagnostic Imaging of Heel Spurs

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Heel spurs are pointed bone lesions at the posterior and inferior contour of the calcaneus. They are 4-6 mm long spikes with a broad base.
The incidence of heel spurs in the mideuropean population is up to 8-10 % with a predominance of the plantar location. The prevalence increases with age. They are caused by chronic traumatic pressure as in foot deformity or obesity (2).

Pathophysiology
Reactive bone formations occur as part of regressive changes in insertional tendons.
These regressive changes can lead to an inflammatory reaction in the ligamental insertions (enthesiopathy).
The plantar heel spur grows into the plantar fascia along the traction and pressure lines of the calcaneus. Because of the slow growth the plantar spur has a smooth outline, a thin cortex and a regularly structured spongiosa. As part of the inflammatory reaction the trabecular framework gets remodeled with sclerosis and erosive changes.
Between fibrous tissue and cartilage the inflammatory tissue causes bone formation.
On histological examination one can find degenerative signs, collagen necrosis and angiofibroplastic proliferations (1).

History and Findings
Heel spurs are often asymptomatic. In 16% of all cases the patients suffer from increasing stabbing pain after strain, which occurs under the heel and can spread into the foot and lower limb. A local tenderness at the medial contour of the tuber calcanei can be observed.
In the chronic stadium the degenerative fibroostosis caused by heel spurs can lead to a plantar fasciitis which must be differentiated from inflammatory signs due to seronegative spondylarthropathy (2).

Imaging

Conventional Radiography:
The lateral view shows the pointed bone lesion at the tuberculum mediale calcanei, which is a "tractional osteophyt" at the insertion of the plantar fascia (figure 1).

Fig. 1: Lateral radiograph of a plantar heel spur

There is no correlation between the size of the heel spur and the pain it causes.
Radiological signs of the plantar fasciitis are sclerosis and thickening of the periost at the tuber calcanei and a wide plantar fatpad (1, 2).
In summary the radiograph shows the heel spur as a possible reason for chronic complaints and may reveal other bone lesions.

Ultrasound:
The spatial resolution of ultrasound increases with higher frequency and smaller wavelength.
Because of the superficial location of the lesion linear transducers with a high resolution are used (7.5 MHZ). The maximal axial resolution is 0.3-0.4mm. In the acute stadium ultrasound shows the edema of the plantar aponeurosis as decreased echogenicity (3).
Chronic stress leads to thickening of the plantar fascia with intermediate echoes.

Scintigraphy:
Nuclear imaging of fibroostosis is negative. In case of plantar fasciitis one can find pathological uptake at the insertion of the plantar aponeurosis even when the X-ray is still normal. In soft tissue scintigraphy 99m-Tc-Pertechnat (99mTc; requires blocking of the thyreoid gland with perchlorate) or 99m-Tc-Methylenediphosphonate (Tc MDP) is used. The examination is performed with a high resolution scanner in two different image acquisition formats: whole body single pass (lower resolution) or spot views (longer time of acquisition, better resolution). The bone uptake 5-30min. after injection of 99mTc is caused by the hyperaemia, the delayed images (2-4 hours p.i.) show the penetration of 99mTc into the soft tissue because of impaired permeability (4).

Magnetic resonance imaging:
MRI is indicated to detect plantar fasciitis in the presence of chronic complaints and the existence of a heel spur.

Technique:
Calcaneal lesions are shown in sagittal and coronal views. Beside standard T1- and T2-weighted images in spin echo technique, fat suppression is achieved using sequences called short τ inversion recovery (STIR): the contrast can be increased by an initial 180° inversion pulse and selection of an appropriate T1 length. If you choose a T1 of 80-150ms (short τ) the resulting contrast is equivalent to a standard fat suppression. This effect makes the evaluation of bone marrow easier.
An example of a protocol (1.0 Tesla system) is outlined in table 1.

native		**enhanced** (0,1 mmol Gd/kg)	
sagittal	T1 spin echo	*sagittal*	T1 spin echo
	T2 turbo spin echo		
	Turbo STIR		
coronal	T1 spin echo	*coronal*	T1 spin echo

Table 1: Example for an examination protocol for 1.0 Tesla system

MRI findings:
In sagittal and coronal views the normal fascia is a 3mm thick hypointens structure in all sequences. Abnormal is a thickening of 7-8 mm with an intermediate increase of signal intensity in T1- and a hyperintensity in T2-sequences. Soft tissue edema of the plantar fascia and a bone marrow edema of the calcaneus (figure 2) can be detected especially in the fat suppressed STIR sequence. After the injection of contrast media increasing signal intensity in the tendon is shown (5).

Fig. 2: Sagittal MRI, showing a signal increase in the plantar fascia and edema in the calcaneal bone marrow

Conclusion
Its availability and ability to delineate other bone lesions make conventional radiography the method of choice for the diagnosis of a heel spur. Ultrasound is helpful in evaluating the adjacent soft tissue. Although scintigraphy has the highest sensitivity for the detection of fasciitis in the peracute stadium, MRI is recommended for further workup because of its high soft tissue contrast and anatomic resolution, resulting in high sensitivity and specificity. The standardized MRI sequences are especially useful for follow-up.

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Literature Commentary:

Is Low-dose Radiotherapy Useful for Peyronie's disease ?

L. Incrocci, A. Wijnmaalen, A.K. Slob, W.C.J. Hop and P.C. Levendag, Rotterdam:
„Low-Dose Radiotherapy in 179 Patients with Peyronie's Disease: Treatment Outcome and Current Sexual Functioning"
Presented at the 41st ASTRO Meeting 1999 ,
published in Int J Radiat Oncol Biol Phys 47 (2000): 1353-1356.

Purpose: To analyse retrospectively treatment outcome in patients irradiated for Peyronie´s disease.
Methods and materials: The records of 179 patients, median age 52 years, that received radiotherapy (RT) between 1982 and 1997 were reviewed. 78% presented with painful erections and 89% with penile deformity. The symptoms were present for a median duration of 6 months (range, 1-72 months). The RT schedule consisted of 13,5 Gy (9 x 1,5 Gy, 3 fractions per week) using orthovoltage X-rays in 123 patients or 12 Gy (6 x 2 Gy, daily fractions) using electrons in 56 patients. A questionnaire regarding current sexual functioning was mailed to 130 patients whose addresses could be traced; 106 (82%) responded.

Results: At mean follow-up period of 3 months, 83% reported that pain was diminished or had disappeared after RT. Twenty-three percent of patients reported a decrease in penile deformity. Following RT, surgical correction of penile curvature was performed in 29% of patients. No RT-related complications occurred except transient dysuria in 1 patient. Questionnaire data: 72% of patients were currently sexually active, 48% had erectile dysfunction, and 49% expressed dissatisfaction with their current sexual functioning.
Conclusion: Low-dose external RT (12-13,5 Gy) results in relief of pain in the majority of patients with Peyronie´s disease. Improvement in penile deformity was observed, avoiding surgery in a number of patients. No significant RT-associated morbidity was encountered. It is disappointing that almost 50% of patients complain of sexual functioning, but this is presumably not related to radiotherapy.

Comment:

The Peyronie´s disease or induratio penis plastica is a rare benign disease, characterized by indurations of the pars libera of the penis. The etiology and pathogenesis of this disease is not yet completely understood. A proposed model is that Peyronie´s disease is initiated by a trauma with subsequently rupture of microvasculature in subjects with genetic predisposition for fibrosis, together with loss of tissue elasticity as a normal aging process. The result is at least a pathological penile fibrosis with plaque formation and even ossification in advanced disease (1). Because of the hypothesis of an inflammatory etiology empirical medical treatments with oral Vitamin E, Potaba (potassium amino-benzoate), colchicine, tamoxifen, or intralesional injections with verapamil, corticosteroids, or collagenase have been tried with unsatisfactory results (1). Several surgical approaches have been used, from plaque excision with dermal grafting to correction of penile deformity without tissue excision, but results are not more successful than noninvasive approaches (3).
Radiotherapy has been previously reported as a successful treatment modality.
The applied doses reported from literature range between 6 and 25 Gy. Pain, which is in most patients the only symptom, improved in about 70 – 90% of cases. To achieve these results doses from 9 to 12 Gy seem to be sufficient. Concerning the regression of penile calcareous plaques, there is a tendency towards better results with higher total doses applied (4).
The reports from literature of improvement of curvature vary between 6% and 48%. An improvement in erectile and sexual function was reported in 0% to 60% of cases by the patients. Both parameters occur inconstantly and were only qualitatively evaluated. The partly reflect the personal impression of the patients (1).
Reviewing the literature of the last 10 years, it became apparent, that many groups treat their patients with a total dose of about 20 Gy; this also applies to our own patients, treated in Münster (5). The more encouraging are the experiences of Incrocci (1), who showed comparable results with a considerably lower irradiation dose. They could convincingly demonstrate their results with a very large collective of 179 patients.

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F. Bruns, O. Micke (Münster)

German Cooperative Group
Radiotherapy
for Benign Diseases

Abstracts from the Annual Meeting of the German Cooperative Group on Benign Diseases (GCG-BD)

Essen, Germany, 4-5 May 2001

Alfried Krupp Krankenhaus

EXPRESSION OF BRADYKININ RECEPTORS IN HUMAN HF-15 CELLS AFTER COBALT-60 IRRADIATION

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Introduction: The peptide hormon bradykinin belongs to the most potent mediators of pain and inflammation. Its effect is mainly mediated by the bradykinin B2 receptor. The influence of ionizing radiation on this system of inflammation mediators has not been analyzed sufficiently so far.
Material and methods: Cultured human preputial fibroblasts (HF-15) were irradiated by cobalt-60 radiation with single doses of 0.5 Gy, 2 Gy, 5 Gy, and 10 Gy. At the points 0, 6, 24, and 48 hours after irradiation, the expression of the bradykinin B2 receptor was determined using a 3H bradykinin binding assay.
Results: For the doses of 2 Gy, 5 Gy, and 10 Gy, the bradykinin B2 receptor showed its highest expression after 6 hours. After 12, 24, and 48 hours, the receptor expression decreased significantly. For the lowest dose of 0.5 Gy, we found a biphasic development with a significant decrease in bradykinin receptor expression after 6 hours relative to the non-irradiated control. An further increase was found after 12, 24, and 48 hours.
Conclusions: For a radiation dose of 0.5 Gy, we found a biphasic development that has already been described for several other inflammation mediators. Our results lead to implications for radiobiological explanations of the radiation effect in benign diseases like inflammatory or degenerative joint diseases.

GRAVES' OPHTHALMOPATHY: RADIATION DOSE THAT DOESN'T REACH THE TARGET TISSUE CANNOT HAVE ANY EFFECT

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Introduction: So far there has only been little research on dose-effect relationships in the radiotherapy of benign diseases. Recommendations for irradiation techniques and simulator planning of Graves' ophthalmopathy are mainly derived from historic experience.
Methods: Three common recommendations for irradiation technique in Graves' ophthalmopathy were analyzed using a three dimensional computer planning system, and the corresponding dose distributions were calculated.
Results: Even when an ideal reproducibility of daily treatment setup is assumed, small fields can only reach part of the orbit with the full prescribed dose.
Great clinical importance is assigned to the external bulbar muscles. The complete inclusion of the medial rectus muscle, which is affected most often, did not pose a problem for any of the three analyzed recommendations. The superior and inferior rectus muscle however often receive only part of the prescribed dose. This is especially true for individually modified portals that are collimated close to the radiological contour of the orbit.
When current recommendations for the inclusion of geometric variations ('margins') are taken into account, all simulator planned fields that are smaller than 5.5 x 6.5 cm possess a very inhomogeneous dose distribution.
Conclusion: When the dose distribution is viewed in three dimensions, small simulator planned fields reach the orbit only inhomogenuously. When daily setup variations are taken into account, clinically important parts of the orbit only receive doses that are markedly lower than the prescribed dose. All further studies on the dose-effect relationship must be based on the spatial dose distribution and practice sufficient quality assurance.

RADIOTHERAPY FOR EPICONDYLITIS RADIALIS HUMERI – A DOSE OPTIMIZATION STUDY (0,5 GY VS. 0,3 GY)

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Background: Radiotherapy is a very effective and low risk therapeutic alternative in the treatment of epicondylitis. Recommendations from literature range from 0.5 to 1.5 Gy (single dose) resp. 3.0 to 9.0 Gy (total dose). A reference dose standard has not been developed so far. In a prospective, randomized study, we compared the long term effect of a common dosage scheme (group A: 0.5 Gy single dose/6.0 Gy total dose) with a low dose scheme (group B: 0.3 Gy single dose/3.6 Gy total dose).
Material/Methods: During the period from 4/1996 to 6/1997, 166 patients with 190 elbows (24 patients with double-sided symptoms) were randomized into one of two dose groups (group A: 91 patients/105 elbows; group B: 67 patients/77 elbows).
Results: With a median follow up of 34.5 months (mean patient contacts: 3.9), 70% of patients of both groups reached a major improvement of symptoms (with only minor complaints remaining) or complete freedom from pain. 55% (group A) and 56% (group B) became completely free from pain. 40% of patients of both groups reached this result after the first series. In 15% resp. 16% of patients, a further treatment series was necessary to reach complete freedom from pain. 6% of patients suffered from recurring pain after they had reached complete freedom from symptoms. Immediately after the end of therapy, only a small fraction of patients of both groups were permanently free from pain, and even after 6 months the reduction of pain was usually not complete. Three months after the end of therapy, the success rate in group A was 13%, compared to 2% in group B. In the following months, the cumulative success rates of both groups converged.
Conclusion: In our study, low dose radiotherapy (0.3 Gy single dose) of epicondylitis was isoeffective compared to conventional dosage (0.5 Gy single dose). We could show that long term results of dose reduction by 40% were identical to those of conventional fractionation, but the therapeutic effect was reached later.

PREOPERATIVE IRRADIATION WITH PAIN-ADAPTED APPLICATION OF NON-STEROIDAL ANTIRHEUMATICS FOR PREVENTION OF HETEROTOPIC OSSIFICATION AFTER TOTAL ENDOPROTHESIS OF THE HIP. RESULTS OF A PROSPECTIVE STUDY.

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Background: The efficacy of preoperative irradiation for the prevention of heterotopic ossifications (HO) after total endoprothesis (TEP) of the hip has been proven by several studies. In the majority of these studies, despite logistic problems, irradiation is carried out 4 hours before surgery. In this prospective study, a

combination of radiotherapy on the evening before the day of surgery and postoperative pain-adapted application of non-steroid antirheumatics (NSAR) was analyzed.
Methods: In 1996, 244 patients without obvious risk factors received radiotherapy with a single dose of 7 Gy 16 hours before implantation of a hip TEP. 92% of these patients additionally received a pain-adapted NSAR therapy for 1 to 4 days after surgery. X-rays were taken on the day after implantation and 3 months postoperatively and evaluated using the HO classification by Arcq. 328 patients who also had received pain-adapted NSAR treatment but no radiotherapy during the year 1993 served as a historic control group.
Results: The incidence of HO over all grades was 21.3% in the control group (70 pats.). Of these, 9.4% (31 pats.) had Arcq grade I, 7.3% (24 pats.) Arcq grade II, and 4.6% (15 pats.) Arcq grade III. In the radiation group, HO developed in 7.7% (19 pats.). Of these, 6.1% (15 pats.) had Arcq grade I, 1.2% (3 pats.) Arcq grade II, and 0.4% (1 pat.) Arcq grade III. Over all HO grades, we could show a significant difference between both groups ($p<0.05$) with an advantage for the irradiated group. Especially the incidence of the clinically relevant Arcq grades II and III could be reduced by radiotherapy.
Conclusion: The combination of preoperative radiotherapy the evening before TEP implantation with pain-adapted NSAR for 1 to 4 days postoperatively reduces the incidence of HO and results are comparable to radiotherapy 4 hours before surgery.

RADIOTHERAPY OF PERIARTHROSIS HUMERO-SCAPULARIS (PHS), EPICONDYLOPATHIA HUMERI (EPH) AND HEEL SPUR WITH 6 MEV PHOTONS.

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Background: Data from literature show subjective pain alleviation in up to 75% of patients irradiated for PHS, EPH, or painful heel spur. Can comparable results be obtained using objective score systems?
Methods: We performed a retrospective analysis of subjective statements from 63 patients with heel spur, 45 patients with PHS, and 39 patients with EPH irradiated during one year. Radiotherapy of all three diseases was done with single doses of 1 Gy three times a week using 6 MeV photons up to a total dose of 6 Gy. Simultaneously, a prospective analysis is being done where it is planned to include a total of 150 patients suffering from the mentioned three diseases. Currently, 14 patients with EPH, 19 patients with PHS and 43 patients with heel spur have been prospectively evaluated. Objective scoring was performed using standardized orthopaedic scoring systems: for PHS we used the score by Constant and Murley, for EPH the score by Morrey et al., and for the heel spur a modified clinical score which was initially introduced by Rowe for calcaneal fractures.
Results: In the retrospective analysis, 42 out of 63 patients painful with heel spur (66%) reported a marked pain alleviation; prospective evaluation using the validated score yielded 30 out of 43 patients (70%). For PHS, the retrospective data for pain alleviation were 30 out of 45 (66%), validated scoring yielded an improvement in 15 out of 19 patients (79%). In EPH patients, 18 out of 39 patients (45%) were retrospectively assigned considerable improvement, while the validated score yielded 11 out of 14 patients (79%) .
Conclusions: For the patients included up to now, the current prospective investigation shows nearly identical results to the retrospective analysis for the treatment of painful heel spurs, PHS and EPH showed even better results than in the retrospective evaluation. The prospective results from EPH and PHS have to be taken as preliminary because of the relatively low number of cases. However, the current comparison indicates that pain alleviation can be detected in up to ¾ of patients and that these results are compatible with those obtained using internationally renowned objective scoring systems.

X-RAY DEPTH THERAPY OF TRIGEMINAL NEURALGIA – EFFECT AND LONG TERM RESULTS – AN ANALYSIS OF PATIENTS TREATED FROM 1989 TO 2000

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Purpose: To determine the value of x-ray depth therapy in the treatment of trigeminal neuralgia by a retrospective analysis of our patients.
Patients and Methods: Of 62 patients treated for trigeminal neuralgia from 1989 to 2000, 48 patients could be included in the analysis using data from their records and a retrospective questionnaire. They consisted of 16 men and 32 women with a mean age of 58 years (34 to 79 years). In 15 patients (31%), symptoms had been persisting for more than one year. All patients had been extensively pre-treated with drugs. Diseases of the mouth and paranasal sinuses had initially been excluded. The right side was affected in 28 cases, the left in 20 cases. In 31 patients, one trigeminal branch was affected, in the remaining 17 patients, more than one branch caused the problem. Irradiation of the ganglial region and the peripheral nerves analogous to the recommendations by SCHERER (Handbook of medical radiology vol. XVII) was performed using an orthovoltage unit with 175/200 kV tube voltage. The single doses were 0.5 Gy (n=4) and 1 Gy (n=44). Using 2 to 3 fractions per week, total doses of 3.0 Gy (n=4), 4.0 Gy (n=8), and 6.0 Gy (n=36) were applied. 9 patients (19%) received a second series because of initial treatment failure.
Results: 17 patients (35%) complained about substantial pain increase during treatment. Immediately after the first series however, 54% of patients reported a positive treatment effect in the form of pain relief. This fraction was increased to 81% after 3 months (no symptoms: 12%; considerably improved: 42%; improved: 27%). After a mean follow-up of 41 months (maximum 107 months), 28 out of the 39 patients (72%) who had experienced substantial pain relief suffered from – usually early – recurring pain (16 patients during one year). We also observed long term remissions in some of the patients (up to 77 months).
Conclusion: The presented analysis supports the positive analgetic effect of x-ray depth therapy in the treatment of trigeminal neuralgia. Roughly half of the patients with initially successful therapy profit from a long term effect of over 12 months.

BENIGN NEWS FROM THE NET

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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 like television, CD-ROM, DVD, and last but not least the Internet and the World Wide Web, the old ways of communication have changed drastically. This change does not only influence the channels of information for the private household as well as for business and government use, it also affects the scientific community as well as the ways of patient information. In a recent survey in Germany, a total of 26.6% of tumor patients received information on their disease directly or indirectly from the internet. All these new means of communication and information retrieval also influence the way a scientific working group should present itself to the public.
This is the reason why we put up a homepage for BenigNews, which can be found at www.benign-news.de. Our homepage currently shows you an overview over the first BenigNews issue as well as full text links to all issues. Protocols of working group meetings are also available online. The complete set of instructions for authors for BenigNews can be downloaded. Announcements of important events in the field of radiation therapy for benign diseases are presented. Questionnaires and documentation sheets are available as well as tables with important facts like the excerpt of the ICD-10. Finally, we have also added a counter showing that our page has received over 250 hits since October 2000.

Additionally, the BenigNews homepage has been submitted to most major search engines.
So these are the first news from our our activity in the Net; hopefully they may be some importance to scientific community and clinical practice alike.

Case report:
RADIOTHERAPY OF AN ADVANCED, MULTIMODALLY PRETREATED HEMANGIOMA OF THE CAVERNOUS SINUS AND THE LEFT FACIAL HALF USING COBALT-60 IRRADIATION – A CASE REPORT

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Background: For cerebral blood vessel malformations, surgical and interventional radiological methods are the predominant therapeutic options. An alternative possibility of vessel obliteration is opened up by modern stereotactic radiotherapy in specialized centers, especially for small and medium size lesions. For larger lesions and in the case of failure of conventional methods, literature only offers singular case reports, especially concerning the optimal and necessary dose, taking into consideration the possible late effects.
Patients/Methods: In a 40 years old man, since early childhood, an AV malformation of the left facial half was known. It consisted of multiple fistulas and angiomas in the middle face (vertebral artery, cavernous sinus, ophthalmic artery). After several bleeding complications, initially leading to cosmetic, finally to mutilating surgery up to exenteration of the orbit, he did not suffer from further complications for several years. In November 1999, he started to suffer from massive bleeding from the nose and pharynx without any endoscopically identifiable source. Radiological interventions using repeated embolization of the diffuse fistulas in the cavernous sinus region did not lead to a sufficient success, the need for blood transfusions was tremendous (26 red blood cell concentrates over 3 months). Any further efforts of embolization were excluded because of possible injury to the right eye with imminent sight loss. As a last resort, the patient was referred to the radiotherapy department for irradiation of his advanced lesions. As an exact localization of the source of bleeding was not possible, we decided to include the complete left half of the patient's face, up to the border of the contralateral orbit, into the target volume, while carefully sparing the right eye itself. At the cobalt-60 unit, we applied a total dose of 18 Gy (prescribed at the 85% isodose) at 4 fractions per week with single doses of 1.8 Gy using parallel opposed fields.
Results: The treatment was very well tolerated, the patient only suffered from intermittent and meanwhile completely dismissed taste irregularities. The last bleeding occurred 2 days after the start of radiotherapy; the patient has been free from any symptoms ever since over a follow-up period of 14 months now.
Conclusion: Conventionally fractionated percutaneous radiotherapy with a total dose of 18 Gy (85% isodose) is an effective treatment even for advanced arterio-venous malformations with little if any side effects.

Case report:
RADIOTHERAPY OF NEUROSARCOIDOSIS

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Background: Cerebral involvement is found in patients with systemic sarcoidosis in about 5% of cases. When the response to steroids remains insufficient, the usual measure consists in modifying the immunosuppressive therapy. Irradiation of the neurocranium can also sometimes be sensibly used in this situation.
Case report: We report about a 49 years old male with an 8 years course of systemic sarcoidosis. After the initial treatment in 1991, the patient first presented with neurological symptoms in 1996 in the form of increased intracranial pressure. Because of the suspected diagnsosi of a primary brain tumor in the left temporo-occipital region, supported by MRI findings, a subtotal resection was performed. Postoperatively, after the definitive diagnosis of neurosarcoidosis, a systemic treatment with 20 mg/d prednisone was carried out. Three years later, the patient suffered from a cerebral recurrence which showed up clinically as newly occurred vertigo with gait disturbance and progressive sight impairment. MRI showed a progression of the partially cystic lesions in the left temporal lobe and additionally in the caudal portion of the basal ganglia. Because of inoperability, the patient received an irradiation of the whole neurocranium via laterally opposed fields with a dose of 10 x 2.0 Gy over 2 weeks. In the mean time, the patient has been referred to our department again and, in spite of a newly diagnosed systemic recurrence, presented with essentially unchanged neurologic condition and MRI findings in the sense of a "stable disease".
Conclusion: Radiotherapy has been described in the literature as an effective therapy for neurosarcoidosis after the failure of steroid treatment. An entire skull irradiation with 20 Gy/2 weeks is described as sufficient. In the case existing here of a very unfavorable illness progression, radiotherapy was only able to prevent a progression of the cerebral manifestations.

Case Report:
SINGLE DOSE EXTERNAL BEAM IRRADIATION IN A PATIENT WITH RESTENOSIS OF AN ILIACOFEMORAL BYPASS GRAFT

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Introduction: The potential role of external beam radiation therapy (EBRT) in preventing neointimal proliferation after vascular injury in atherosclerotic artery disease is still an issue of controversy, because beneficial as well as detrimental effects have been reported. We report on a patient who received EBRT because of a recurrent thrombotic occlusion of an iliacofemoral bypass graft due to a large neointimal hyperplasia.
Case report: A 54 year old male was admitted in July 2000 because of claudication. He had a history of Ormond' s disease and an iliacofemoral bypass graft was implanted in May 2000 because of atherosclerotic vascular disease. Recurrent thrombotic occlusions occurred during a 7 day period, so that surgical thrombectomy was performed. A large neointimal hyperplasia at the distal anastomosis of the bypass graft was resected. Logistic restraints precluded immediate intraluminal brachytherapy, so that an external beam approach was performed 24 hours later. A single dose of 16 Gy was delivered. The patient was well until march 2001 when claudication returned. Catheter directed thrombolysis restored bypass perfusion completely. Angiography showed a moderate stenosis of the anastomosis with sufficient runoff flow.
Discussion: EBRT in peripheral vascular disease is an uncomplicated and readily available modality. Although there is some advantage for intraluminal brachytherapy, the potential role of EBRT in restenosis prevention should be carefully examined. It may be applied to a spectrum of vascular restenosis pathology, particularly in situations where intraluminal therapy is not immediately accessible.

Case Report:
RADIOTHERAPY FOR GORHAM-STOUT SYNDROME

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Introduction: Gorham`s disease is known to be a very rare idiopathic osteolysis (since 1838 only about 200 cases were reported in the literature). It is characterized by the replacement of bone with lymphangiomatic tissue.

Case report: A ten year old boy developed increasing painless neckstiffness without any incident of trauma. Initially conventional X-rays showed a single manifestation of osteolysis. Furtheron more cervical spinal vertebrae were affected. Within 5 years the osteolytic process extended from the base of the skull to the upper thoracic spine and ribs. 4 years after the beginning of the disease the patient developed a pericardial effusion and massive persisting chylous pleural effusions. In this stage radiotherapy was initiated. A total dose of 36 Gy was delivered (5 x 2 Gy/week). The irradiated volume extended from the base of the skull down to the sixth cervical vertebra. In addition the upper thoracic region was irradiated. During therapy pain could be reduced significantly. However, the patient died 6 months later due to cardiac failure and pleural effusions.
Discussion and Conclusion: Gorham`s disease advances locally. The involvement of the osseous thoracic structures may cause pleural effusions which may be lethal like in this case. In the literature, the most important therapeutic options are surgery and radiotherapy. As the disease is rare, the different treatment options are discussed controversely. Radiotherapy generally leads to a quick pain reduction as well as to a recalcification of the destroyed bony structures if it is started in time. A total dose of 35 to 40 Gy is recommended.

Case Report:
SYSTEMIC MASTOCYTOSIS AND BONE PAIN - A CASE TREATED WITH RADIOTHERAPY

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Introduction: Systemic mastocytosis is a rare disease characterized by mast cell infiltration of organs. Bony pain is present in up to 28% of cases and is frequently chronic and difficult to palliate with medical therapy.
Patient and Method: We report one case of refractory bone pain in a female patient with advanced systemic mast cell disease and associated bony involvement, which was treated with radiotherapy. Between 1995 and 1998, the patient was irradiated at four different locations (right shoulder, both hands, both knees, left upper arm and shoulder) with a dose of 40 Gy in 2,0 or 2,5 Gy daily fractions.
Result: Different results of pain control were achieved. In one location the pain was reduced for 57 months until her death due to disease progression, whereas in two other location a pain control was maintained for 3 and 6 months. In one location, no pain reduction was achieved. Severe side-effects were not observed.
Conclusion: Palliative radiotherapy has a role in the control of severe intractable bone pain in patients with advanced mastocytosis, though in some cases the effect may be short or incomplete. The observed palliation of pain can even differ in the same patient.

Case Report:
OUTCOME OF RADIATION THERAPY AND INTERFERON ALPHA IN A NEONATE WITH KASABACH-MERRITT SYNDROME

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Introduction: The optimal therapy for Kasabach-Merritt syndrome is still controversial. We describe the successful treatment of a neonate with Kasabach-Merritt syndrome who received local irradiation and interferon alpha therapy after failure of corticosteroid treatment. Patient and Method: A male neonate, born after an uneventful pregnancy had a huge hemangioma extending the upper right cervical region and severe thrombocytopenia. He was treated with corticosteroids, interferon alpha and radiotherapy. Prednisolone therapy (5mg/kg/day) was started at 41 days of age. No therapeutic effect was observed after two weeks; the tumour size had increased dramatically, platelet counts had progressively decreased and coagulation abnormalities had developed. Because corticosteroid therapy had been ineffective and the child was in a life-threatening condition, irradiation was delivered up a total dose of 9,5 Gy in 5 fractions. Simultaneously, prednisolone therapy was slowly decreased and a therapy with interferon alpha therapy (3 million U/m^2/day) was started and continued for 6 weeks.
Result: After irradiation with 9,5 Gy and the beginning of an interferon alpha therapy, the tumour decreased in size and coagulation parameters normalized within 4 weeks. 6 months later, platelet counts and coagulation parameters were still normal. The tumour had further decreased in size. No acute severe side-effects were observed.
Conclusion: Radiation therapy combined with interferon alpha treatment are an alternative treatment modality when high dose corticoid steroid therapy has been ineffective in patients with Kasabach-Merritt syndrome despite the risks of growth delay and secondary malignancy. In children without response to corticosteroids, radiotherapy and/or interferon alpha should be considered in Kasabach-Merritt syndrome.

Awards:

The Paul-Krause-Award of the Rhinish-Westfalian Roentgen-Society

Radiobiological Studies on the effect of external beam irradiation on neointimal proliferation in a rabbit model

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Restenosis after catheter-based revascularization has been demonstrated to be primarily caused by smooth muscle cell proliferation. This study examined in several steps the effects of external beam irradiation on neointimal hyperplasia in a rabbit model.

40 male New Zealand White rabbits were used in the first step. External crush lesions were performed with kelly clamps on each ear under general anesthesia and bilateral auricular nerve blockade. A single dose of 12 Gy (n=10), 16 Gy (n=10), or 20 Gy (n=10) and a fractionated dose of 20 (4x5 Gy) x-ray was delivered to the left or right central artery of the ear 24 hours after injury; the contralateral central artery served as control. All rabbits were sacrificed after twenty-one days and the central arteries of both ears were fixed for morphometric measurements. Morphometric measurements were carried out using computer-assisted planimetry. In a second step, 15 male rabbits were used for immunostainings. A single dose of 16 Gy x-ray radiation was delivered to the left or right central artery of the ear 24 hours after injury; the contralateral central artery served as control. Rabbits were sacrificed after four, fourteen and twenty-one days. Immunostaining for endothelial cell (CD31), macrophages (RAM11) and SMC alpha-actin (HHF35) was performed to determine radiation-induced changes. 10 rabbits were used in a third step for a long time follow-up. Crush lesions were performed as mentioned above, animals were treated with 16 Gy single dose and sacrificed after 6 months.

Animals treated with a single dose of 16 Gy or 20 Gy showed a significant reduction in neointimal proliferation of the irradiated site compared with the unirradiated control, a less prominent, not significant effect was noted for the 12 Gy and 4x5 Gy group. In the immunostainings, no delayed reendothelialization was observed (CD31). SMCs immunoreactive to anti-SMC alpha actin were found in the neointima and media, but not in the adventitia (HHF35). Macrophages were observed after 4 days, but no difference was found between the 16 Gy group and control (RAM11). Long term follow-up showed no delayed neointimal proliferation after a period of 6 months.

This multistep analysis could demonstrate, that X-ray irradiation with 16 or 20 Gy is successful in long term reducing of neointimal hyperplasia, lower radiation doses are less efficient. Vessel irradiation does not delay reendothelialization and no evidence was found that macrophages are target elements for radiotherapy. In this model, the role of the adventitia remains unclear.

Dr. Ulrich Schäfer, consultant physician at the Department of Radiotherapy and Radiation Oncology of the University Hospital of Münster, achieved the Paul-Krause-Award of the Rhinish-Westfalian Roentgen-Society endowed with € 5000,- for his work "Radiobiological Studies on the effect of external beam irradiation on neointimal proliferation in a rabbit model"

(Extended contribution see left)

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.

The best article per year is awarded with € 50,-!

INSTRUCTIONS FOR AUTHORS

This text represents an excerpt from the full authors' guidelines which is available at http://www.benign-news.de.

Official Language
The official language of the newsletter is English. Help will be provided for translation if required. Please contact the publishing office.

Papers and correspondence should be submitted to:
Dr. Oliver Micke, Managing Editor and Publishing Office, Diplodocus-Verlag, Grüner Weg 24c, 48341 Altenberge, Germany,
E-mail: omicke@diplodocus-verlag.de,
Phone: +49 2505 947458 or +49 251 8347839, Fax: +49 2505 947463

Types of Articles
1. *Original papers (full length)*
   The article should deal with original scientific work in the field of radiation therapy of benign diseases or related areas. Full papers should be divided into the sections *Introduction*, *Materials and Methods*, *Results*, and *Discussion*. A length of 3 printed pages, including 3 tables or figures, should not be exceeded.
2. *Short communications and technical notes*
   These papers should include a brief summary of a particular topic and usually not exceed 2 printed pages and 2 tables or figures.
3. *Reviews and overviews*
   The submission of reviews and overviews is strongly encouraged, as BenigNews is primarily an information letter. For other information see under 2.
4. *Editorials and comments*
   Will usually be done on an invited basis. For other information see under 2.
5. *Letters to the editor*
   On topics of current interest or on previously or simultaneously published material. A limit of 300 words should be obeyed. 1 table or figure can be included.
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.

Next Meeting of the German Cooperative Group on Benign Diseases (GCG-BD)

03.05.–04.05.2002

Alfried-Krupp-Krankenhaus, Essen

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"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

8.09-11.09.2001
7. Jahreskongress der Deutschen Gesellschaft für Radioonkologie (DEGRO2001)
in *Hamburg, Germany.*
Contact: Prof. Dr. med. W. Alberti
Secretariat: Henning Rohwer, Tel.: +49 (0)40/42803-5987, Fax: -5192
Abteilung für Strahlentherapie und Radioonkologie
Klinik und Poliklinik für Radiologie, Universitätsklinikum Hamburg-Eppendorf
Internet: http://www.degro.org
Meeting of the GCG-BD, Refresher Course on Radiotherapy of Benign Diseases

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
Refresher Course on Radiotherapy of Benign Diseases

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 2/2001)
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,
E-Mail: omicke@uni-muenster.de, Internet: http://www.trace-elements.org

25.11.-30.11.2001
87th Scientific Assembly and Annual Meeting of the Radiological Society of North America (RSNA 2001)
In Chicago,
Contact: Internet: http://www.astro.org

Diplodocus-Verlag – Altenberge

Excerpt of Published Books:

M. H. Seegenschmiedt, H.-B. Makoski (Hrsg.):
15. Kolloquium Radioonkologie / Strahlentherapie - Radiotherapie von gutartigen Erkrankungen, Diplodocus-Verlag, Altenberge, 2001, 198 Seiten + Anhang, zahlreiche Abbildungen, Ringbindung, ISBN 3-934870-11-2, 40,- DM

M. H. Seegenschmiedt, H.-B. Makoski (Hrsg.):
10. Kolloquium Radioonkologie / Strahlentherapie - Radiotherapie von gutartigen Erkrankungen, Diplodocus-Verlag, Altenberge, 2000, 196 Seiten, zahlreiche Abbildungen, Ringbindung, ISBN 3-934870-00-7, 40,- DM

M. H. Seegenschmiedt, H.-B. Makoski (Hrsg.):
4. Kolloquium Radioonkologie / Strahlentherapie - Radiotherapie von gutartigen Erkrankungen, Diplodocus-Verlag, Altenberge, 2000, 214 Seiten, zahlreiche Abbildungen, Ringbindung, ISBN 3-934870-01-5, 40,- DM

M. H. Seegenschmiedt, H.-B. Makoski (Hrsg.):
2. Kolloquium Radioonkologie / Strahlentherapie - Radiotherapie von gutartigen Erkrankungen, Diplodocus-Verlag, Altenberge, 2000, 111 Seiten, zahlreiche Abbildungen, Ringbindung, ISBN 3-934870-02-3, 40,- DM

E. Burhoff, K. Forsmann, S. Funke-Hermanny, M. H. Seegenschmiedt (Hrsg.):
Bestrahlungskonzepte bei gutartigen Erkrankungen – Praxisanleitungen für MTRA, Diplodocus-Verlag, Altenberge, 2000, 53 Seiten, zahlreiche Abbildungen, Ringbindung, ISBN 3-934870-06-6, 20,- DM

F.-J. Prott (Hrsg.):
1. Wiesbadener Strahlentherapiesymposium. Strahlentherapie bei Tumoren der Kopf-Hals-Region, Tumoren des Gehirns, mit Beiträgen von R. Engenhart-Cabilic, U. Haverkamp, O. Micke, F.-J. Prott, U. Schäfer, M.H. Seegenschmiedt, W. Wagner & Th. G. Wendt, Diplodocus-Verlag, Altenberge, 2000, 66 Seiten, zahlreiche Abbildungen, Taschenbuch, ISBN 3-934870-07-4, 30,- DM

O. Micke, R. Mücke, J. Büntzel & K. Kisters (Hrsg.):
AKTE. Band 1. Proceedings des Second Münster Workshop on Trace Elements and Electrolytes in Radiation Oncology – AKTE 2/2000. Mit Beiträgen von P. Schüller, F. Zimmermann,, A. de Vries, et al. Diplodocus-Verlag, Altenberge, 2000, 30 Seiten, broschiert, ISBN 3-934870-08-2, ISSN 1615-6507, 39,80 DM

O. Micke, R. Mücke, J. Büntzel & K. Kisters (Hrsg.):
AKTE. Band 2. Proceedings des Third Meeting of the German Working Group Trace Elements and Electrolytes in Radiation Oncology – AKTE 1/2001. Mit Beiträgen von P. Schüller, F. Matzkies, R. Mücke, et al., Diplodocus-Verlag, Altenberge, 2001, 35 Seiten, broschiert, ISBN 3-934870-09-0, ISSN 1615-6507, 39,80 DM

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IMPRESSUM

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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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