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OSTEONECROSIS AND SARCOMA FOLLOWING EXTERNAL IRRADIATION OF INTRACEREBRAL TUMORS

by

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It was long believed that osseous tissue is relatively insensitive to ionizing radiation. The first case of radiation osteonecrosis was published by BAENSCH as late as 1927, since when numerous others have been reported. Most of these radiation reactions have been seen in the femoral neck, mandible, clavicle, spine, ribs and pelvis. KOLÁR & VRABEC (1960) reported 110 personal cases. Aseptic osteonecrosis of the cranium not due to malignancy appears to be rare, for only some 25 cases are on record. The lesion was first reported by BALLI & BARBANTI-SILVA (1931) who also described its histologic appearances. Further cases have been contributed by LOREY & SCHALTENBRAND (1932), CAMP & MORETON (1945), VOGT (1949), KNITTEL (1955), SALVINI (1956), KOLÁR & VRABEC (1957), RÜBE (1957), HAUBRICH & BREUER (1958), FREYER (1959), WACHTLER (1961), BROTSLAVSKIJ (1962), MIRIMOVA & ANDREENA (1962) and LUGER et coll. (1963).

MARIE et coll. (1910) described the induction of osteosarcoma by roentgen

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radiation in animals. The first such cases in human beings were described independently by BECK and by MARSCH in 1922, who reported 3 cases and 2 cases, respectively, of sarcoma of long bones, 3 to 8 years after their irradiation for tuberculosis. The number of published cases of osteosarcoma following irradiation has since increased to more than 100; large series have been published by HATCHER (1945), CAHAN et coll. (1948), SABANAS et coll. (1956), CRUZ et coll. (1957) and GOLDBERG et coll. (1963). Only 5 cases of sarcoma of the calvarium, however, are on record (SKOLNIK et coll. 1956, RAVENTOS et coll. 1960, MEREDITH et coll. 1960, and WENDE 1962). JÆNTZER (1937) induced an osteosarcoma of the cranium in rabbits by the application of radium, and BERG & LINDGREN (1961) described sarcoma of the cranium in the rabbit after roentgen irradiation.

Present material

Osteonecrosis of the calvarium. Roentgenograms of patients who had received a full course of radiation treatment during the period 1946—1958 for primary intracranial tumors were re-examined, and the changes observed were correlated with other findings. Roentgen examination after the conclusion of treatment had suggested osteonecrosis in 25 patients. In four of them, however, the further course indicated that the lesions were of infectious origin (suppuration and migration of sutures within 3 months of completion of treatment), in two the lesions proved to be metastases from medulloblastoma (changes also in other parts of the skeleton within 11 months of the conclusion of treatment), and in one patient re-examination of films taken before therapy disclosed that the changes, though then slight, had already commenced. The roentgenograms in one patient revealed necrosis developing into sarcoma and in another an osteolytic sarcoma without previous necrosis.

The material thus consisted of 16 patients with uncomplicated osteonecrosis and 2 patients (see below) with sarcoma.

Treatment was administered with 170 kV roentgen irradiation. The other radiologic data, sex distribution, age distribution, and the diagnoses for which the 16 patients were treated are given in Table 1. A Thoraeus filter (HVL = = 1.5 mm Cu) was used in two patients and a filter of 0.5 mm Cu + 1 mm Al (HVL = 0.9 mm Cu) in the remaining patients. The skin doses ranged between 1 100 R and 4 500 R, the larger doses usually being delivered in several series of 2 to 4 weeks' duration at intervals of 4 to 6 weeks; one treatment was given daily (except Sundays) with the irradiation of one field per treatment. The intervals between the end of radiation treatment and detection

Table 1

Data concerning 16 patients with osteonecrosis

Patient	Sex	Age yrs	Diagnosis	Total skin dose, R max.	Treatment period in days	Skin dose/ treatment in R	Cumulative skin dose, R, according to STRANDQVIST	Maximal absorbed bone dose in rad	Interval (yrs) between treatment and diagnosis of osteoradionecrosis
A	♂	18	Medulloblastoma	3 300	21	500	1 300	8 000	1
B	♀	18	Medulloblastoma	3 300	70	400	~ 1 000	8 000	9
C	♂	13	Medulloblastoma	4 200	63	300	1 000	10 000	1
D	♂	12	Medulloblastoma	3 200	105	400	~ 900	7 500	2
E	♂	9	Medulloblastoma	4 500	35	300	1 500	11 000	1
F	♀	7	Medulloblastoma	3 000	28	300	1 100	7 000	< 2
G	♀	3	Medulloblastoma	4 200	28	400	1 600	10 000	1
H	♂	53	Astrocytoma	4 000	84	500	1 250	9 500	7
I	♂	50	Astrocytoma	3 300	28	400	1 100	5 500	< 2
K	♀	33	Astrocytoma	4 000	63	500	1 100	9 500	6
L	♂	20	Astrocytoma	3 200	42	400	1 100	5 500	< 1
M	♀	19	Astrocytoma	4 000	63	600	1 250	9 500	4
N	♂	10	Astrocytoma	3 000	42	400	1 050	7 000	1
O	♂	24	Glioblastoma multiforme	3 600	28	500	1 400	8 500	2
P	♀	63	Oligodendroglioma (?)	3 400	28	400	1 250	8 000	< 2
Q	♂	14	Malignant oligodendroglioma	4 000	70	500	1 250	9 500	< 5

of osteonecrosis as well as the course of the lesions are indicated in Fig. 1. Six of the patients (L, P, N, O, C and B) are still living 7, 7, 8, 9, 11 and 17 years after treatment.

Sarcoma of the calvarium after irradiation. In neither of the two cases of sarcoma to be described had any signs of other disease of the calvarium been observed before radiotherapy.

Case 1. A girl, aged 7 years, with cerebral symptoms had roentgen evidence of a central, calcified tumor. In March 1956 the patient was operated upon with subtotal extirpation of a partly intraventricular tumor. Histologic examination revealed a teratoma with development of bone, cartilage and chorioid plexus-like structures. Numerous mitoses and cellular atypia suggesting malignancy were noted.

Postoperative roentgen treatment was given to three 6 cm × 7 cm fields (Fig. 2 a), 170 kV,

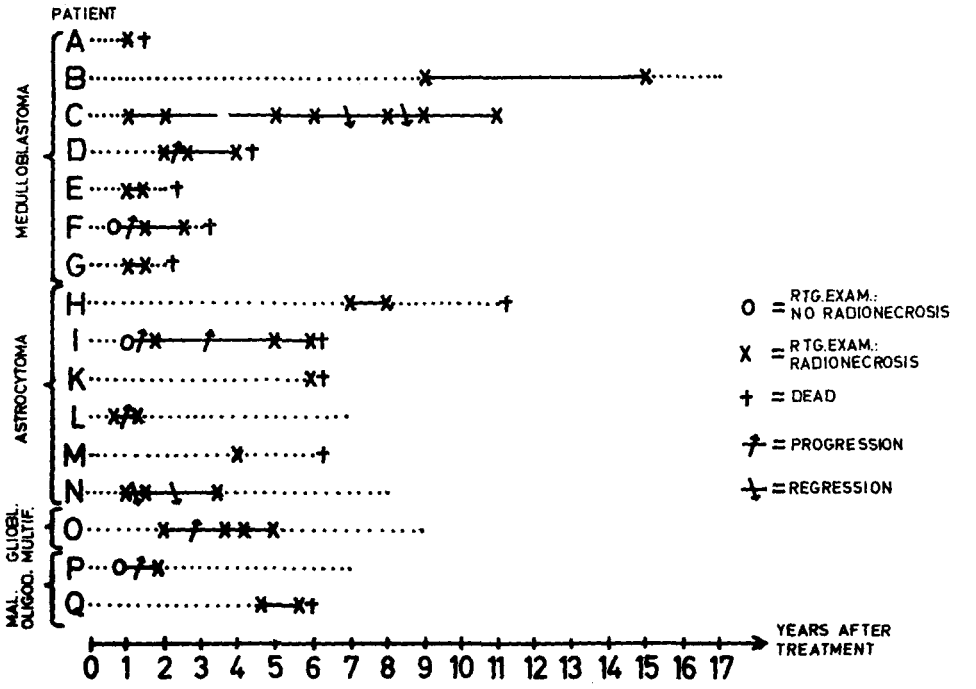


Fig. 1. Course of osteonecrosis in 16 patients.

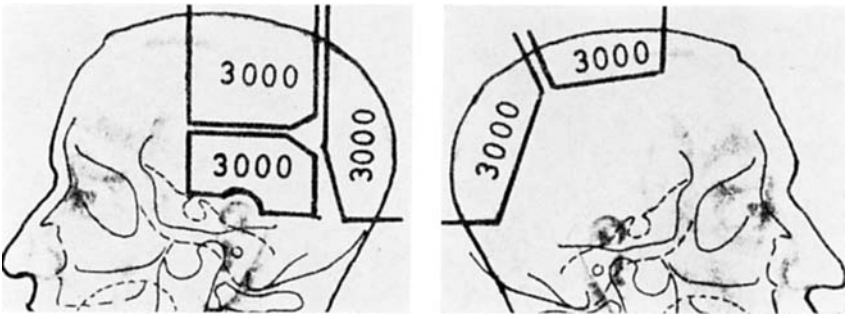
filter 0.5 mm Cu + 1 mm Al and FSD 60 cm for 35 days with a skin dose of 3 000 R, the calculated tumor dose being 3 900 to 4 500 R. The hair began to fall out after the patient had received 1 100 R/11 days, and following treatment the irradiated areas were hairless. The patient afterwards felt well and did well at school.

In the spring of 1962, six years after the conclusion of treatment, a subcutaneous tumor began to grow rapidly in the temporal region down over the bone flap. The patient had headache but no other symptoms. Roentgen examination (Fig. 2, b and c) disclosed *thinning* of the bone in the area treated, as well as patchy, irregular areas of rarefaction suggesting osteonecrosis. Biopsy revealed a sarcoma.

The soft tissue tumor progressed and roentgen examination 7 months and 10 months later produced evidence of progress of the pathologic changes (Fig. 2, d and e). In February 1963 the patient was operated upon with subtotal extirpation of the sarcoma, which was growing into the middle and posterior thirds of the sinus and infiltrating the dura.

Histologic examination revealed pleomorphous sarcoma with formation of collagen fibrils but without definite osteoid tissue (Fig. 3). The patient died 9 months later and no autopsy was performed.

Case 2. A woman who had at the age of 25 developed neurologic signs. Five years later a cerebral tumor was evident in the right temporal region. In November 1958 the patient was



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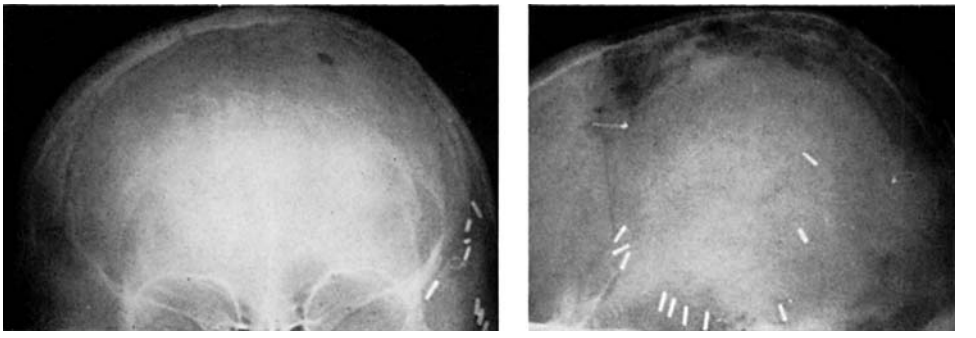

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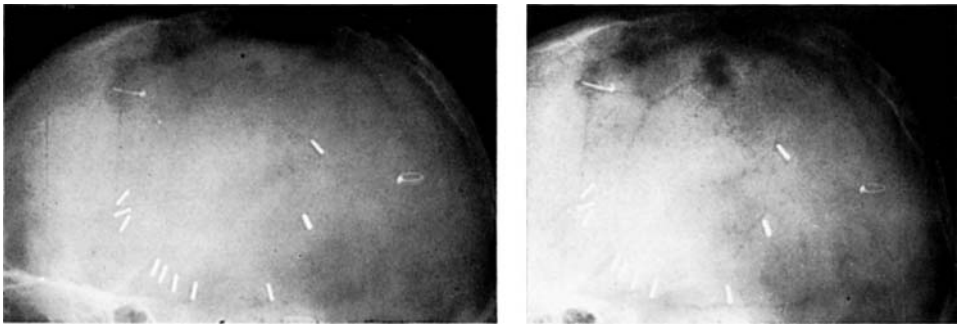


d e

Fig. 2 Case 1. Osteonecrosis and sarcoma. a) Portals and skin doses in R. b) Thinning of bone on left side in the treated area 6 years after conclusion of treatment. c) Lateral projection. Patchy irregular decalcification in the same area. d) Seven months later. Slight increase of the patchy decalcification. e) Ten months later than (b) and one month before operation. Progression of the pathologic changes; no periosteal reaction.

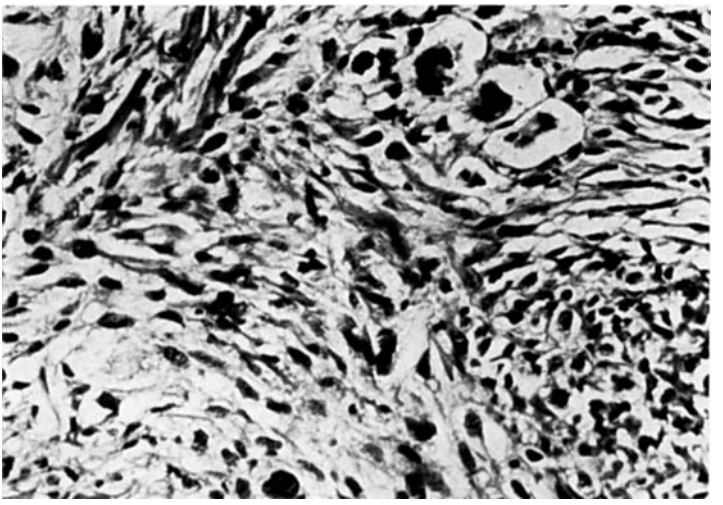


Fig. 3. Case 1. Polymorphocellular sarcoma with scanty fibrous fibers. No definite osteoid tissue. van Gieson. × 250.

subjected to operation with right-sided resection of the temporal lobe and partial extirpation of a mandarin-sized tumor. Histologic examination revealed an astrocytoma of intermediary type.

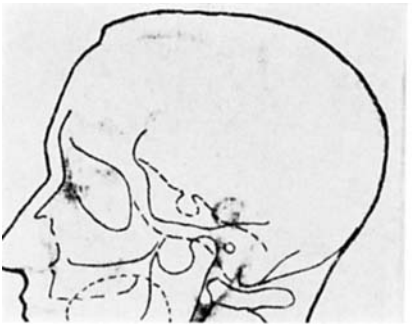
Three months after the operation, by which time the wound had healed well, roentgen treatment was started with 170 kV, filter 0.5 mm Cu + 1 mm Al and FSD 60 cm. Four fields, 5 × 5 to 5 × 6 cm, were irradiated (Fig. 4 a). The skin dose was 2 900 R to 3 850 R and the calculated tumor dose 5 200 R/40 days. The patient afterwards felt well and EEG indicated continuous regression.

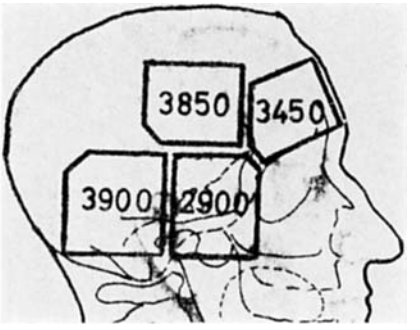
Roentgen examination of the skull in 1959, 1960 and 1961 disclosed no change in the position of the operation cavity as judged by tantalum powder that was introduced. The last roentgen examination of the skull in 1961 revealed osteolytic changes suggesting osteonecrosis (Figs 4c and 5a).

In March 1964, 5 years after the end of roentgen treatment, a tumor began to grow rapidly in the right temporal field, where the skin dose had been 3 850 R/39 days. The patient had no symptoms to suggest recurrence of the cerebral tumor. Roentgen examination in July 1964 (Figs 4d and 5b) disclosed progression of the lytic changes in the bone, and a soft-tissue tumor poor in blood vessels outside the suppressed bone flap. The lamina externa in the area appeared to be irregular.

The tumor was considered to be inoperable and the patient was treated with ^{137}Cs in a dose at 0.12 cm under the skin of 3 000 rad/14 days. The mass then regressed considerably. After the patient had received 1 800 rad, biopsy revealed that the growth was of cartilaginous consistency, shining white and poor in blood vessels. A metastatic lymph node near the right mandibular angle was present.

Histologic examination showed a fibrosarcoma (Fig. 6). When last seen, 4 months after the end of treatment, the patient had pulmonary metastases.





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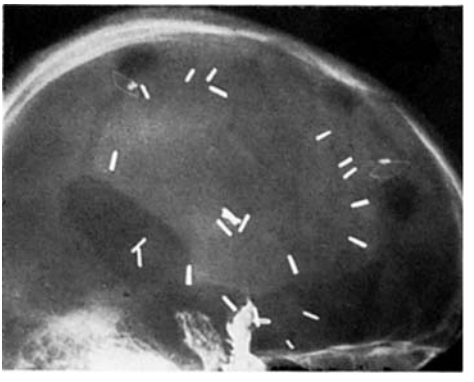

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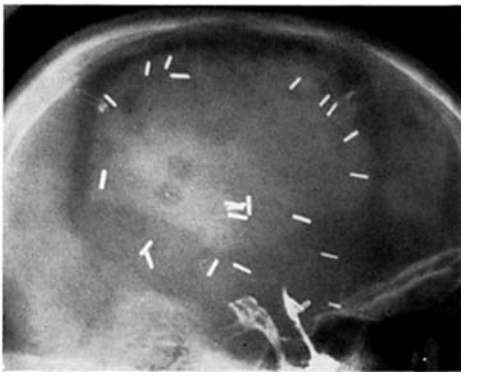

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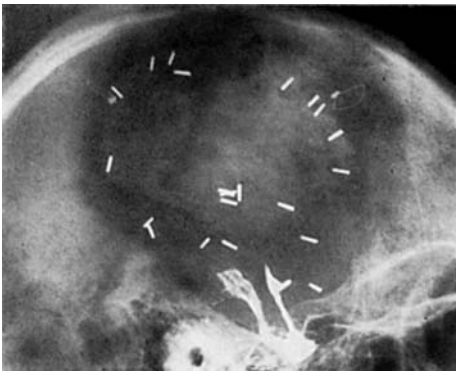
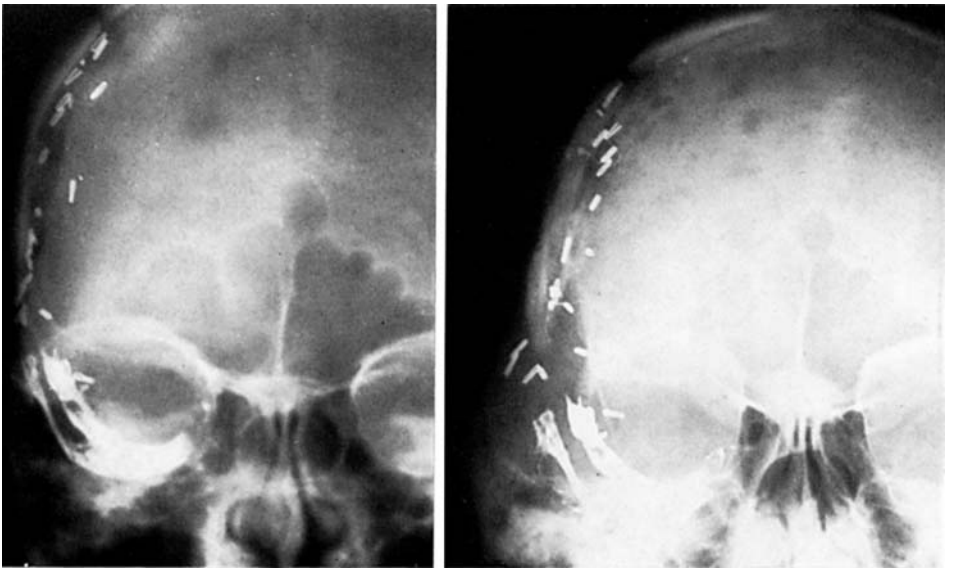


d

Fig. 4. Case 2. Osteonecrosis and sarcoma. a) Portals and skin doses in R. b) Postoperative appearances before roentgen treatment. Operation defects; tantalum powder inserted. c) Two years and 9 months after end of roentgen treatment. Patchy, lytic changes in the flap and neighbouring bone of the area treated. d) Further 2 years and 8 months later. Progression of changes.



a b

Fig. 5. Case 2. a) Frontal projection 2 years and 9 months after end of treatment. b) Frontal projection after further 2 years and 8 months. Displacement of flap medially compared with previous investigation; slight irregularity in tabula externa of flap.

Discussion

Frequency of osteonecrosis. Osteonecrosis (radiation osteitis) of the skull following irradiation has been described in both sexes (7 males, 18 females) and at all ages ranging from early infancy to 60 years. The present material consisted of 10 males and 6 females, aged 3 to 63 years.

Osteonecrosis is probably more common than hitherto supposed. It is well known from clinical experience as well as from experiments by BADE & KÜNTSCHER (1939) that even marked histologic changes of the skeleton are not always roentgenologically demonstrable. The condition per se does not appear to produce any symptoms and probably often runs a subclinical course, causing changes mainly in weight-bearing bones. BORGSTRÖM & GYNNING (1957) reported vertebral compression to be common (12 out of 19) in patients who had survived rotational roentgen treatment for oesophageal cancer for more than 3 years. The commonest site of fracture in necrotic bone is the femoral neck, where the predisposition to fractures is well known. In an epidemiologic investigation, ALFFRAM (1964) gave osteonecrosis as a causal factor of fractures of the femoral neck in only 15 of 1 664 cases.

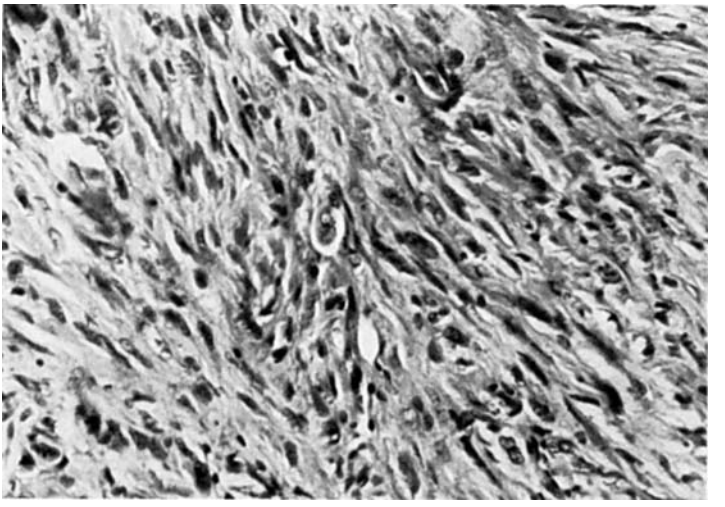


Fig. 6. Case 2. Relatively well differentiated fibrosarcoma with delicate fibrils in the intercellular substance. Haematoxylin and eosin. × 250.

The frequency of osteonecrosis varies from series to series. CAMP & MORETON (1945) found 5 instances in 2 046 patients who had received roentgen radiation therapy for intracranial tumors but they stress that only a few were followed up roentgenographically. KNITTEL (1955) reported necrotic changes in 9 out of 28 patients. The poor prognosis of such tumors makes it difficult to assess the true incidence of necrosis.

The present series of osteonecrosis included 7 patients with medulloblastoma and 6 with astrocytoma. During the same period, 35 patients with medulloblastoma and 55 with astrocytoma (Fig. 7) had received roentgen treatment. Osteonecrosis was thus demonstrated in 20 % of the patients with medulloblastoma and in 11 % of those with astrocytoma. Since the 3-year survival rate of the two groups was 20 % and 75 %, respectively, the frequencies observed for osteonecrosis must be minimal, especially since some of the 35 patients with medulloblastoma were not examined roentgenographically after radiotherapy. The discrepancy between the frequency of necrosis in the two groups may be explained by differences in age distribution (Fig. 7), the radiosensitivity of the neurocranium being higher in early age.

Onset and course. Most records indicate that the patients were not regularly examined roentgenographically after the conclusion of radiation treatment. The reports are therefore of only limited value in the assessment of the latency of osteonecrosis, but changes have been described 1 to 20 years after treatment.

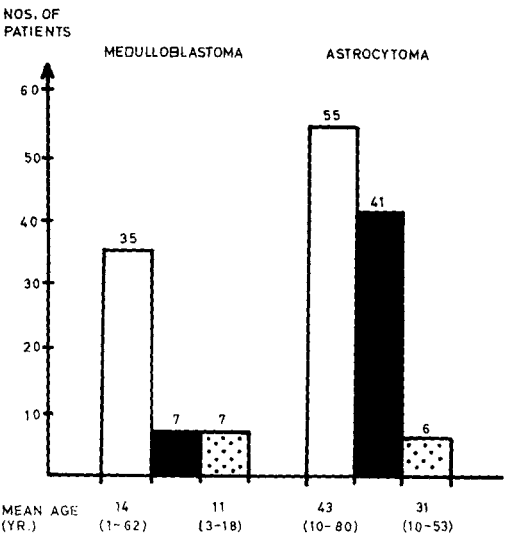


Fig. 7. Number of patients given roentgen treatment between 1946—1958 with 3-year survival. Frequency of uncomplicated osteonecrosis and age distribution are given.

SALVINI (1956) and WACHTLER (1961) observed that the changes progressed for 1 to 4 years after the end of treatment, and re-examination after a further interval of 1 to 3 years revealed no further progression. According to KOLÁR & VRABEC (1957), additional irradiation stimulates progression of the necrotic changes. None of the patients of the present series received further irradiation of the cranium.

Since 1950, roentgenograms have been obtained regularly after treatment in the present series. The course was followed roentgenographically for several years in eight of the 16 patients but for only a short period or only on one occasion in the remaining eight (Fig. 1). Roentgen examination at 8, 12 and 9 months, respectively, after the conclusion of treatment in patients F, I, and P, respectively, disclosed no signs of osteonecrosis. Such changes were, however, evident on examination 18, 21 and 22 months after treatment. In the remaining 13 patients, osteonecrosis was demonstrated roentgenographically at the first follow-up examination after the conclusion of treatment. The first roentgen examination after treatment in six (A, C, E, G, L and N) of these 13 patients was performed one year after the end of treatment. Bone necrosis was thus discovered within one year after treatment in 6 patients, after 18 months to 3 years in 5, and after more than 3 years in the remaining 5 patients.

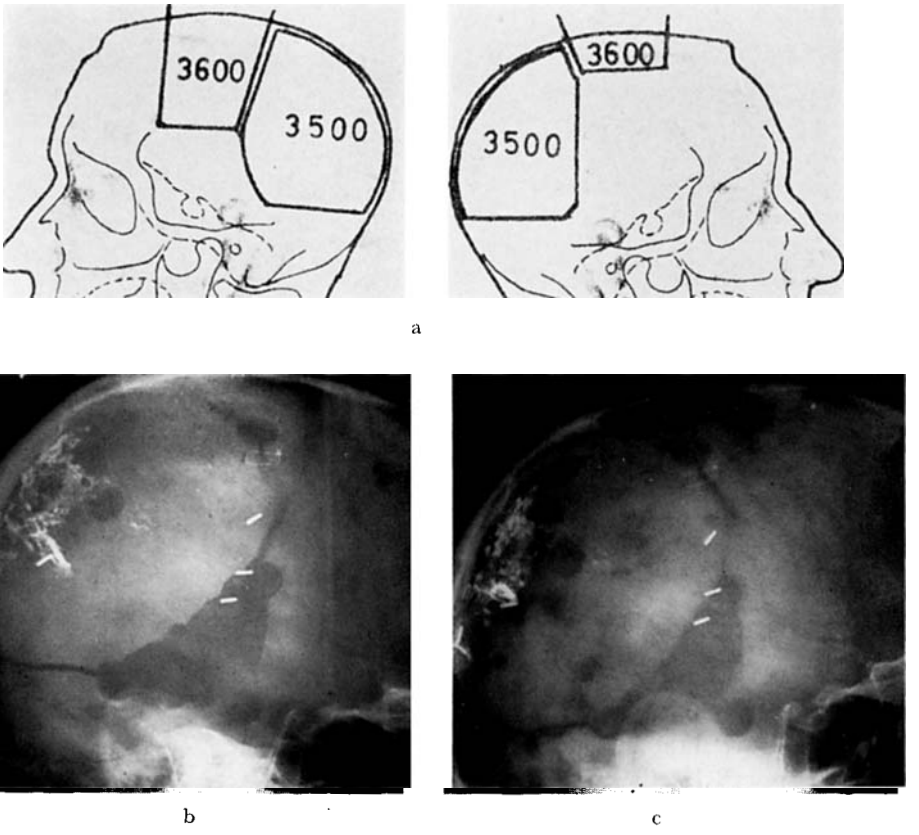


Fig. 8. Osteonecrosis in patient O (see Table 1). a) Portals and skin doses in R. b) Immediately after end of roentgen treatment. Operation defects; tantalum powder inserted. c) Three years and 8 months later. Widespread patchy decalcifications in the areas treated.

The course was followed from 7 months to 5 years following the end of treatment in six patients (D, F, I, L, O and P) in whom necrosis progressed. Fig. 8 represents the development of osteonecrosis in patient O. Supervening necrosis was also noted in patients D and O, but in patient B the necrosis was stationary from 9 to 15 years after treatment. The changes became static as early as one year after treatment in four patients (C, E, G and N) and in two of them (C and N), in whom the course was followed for several years, the changes even regressed in that they became smaller, more calcified and less distinctly outlined. Figs 9 and 10 depict the course in patient C. Although regression of osteonecrosis of the cranium has not previously been described it is recognized that fractures of radionecrotic bone may heal (BIRKNER 1953).

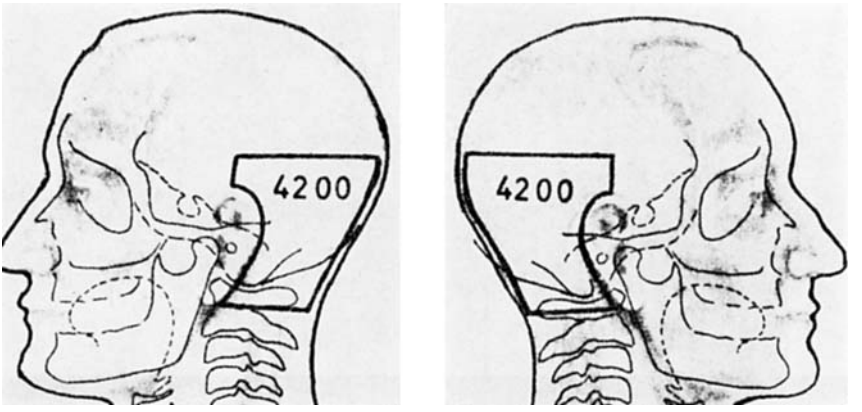
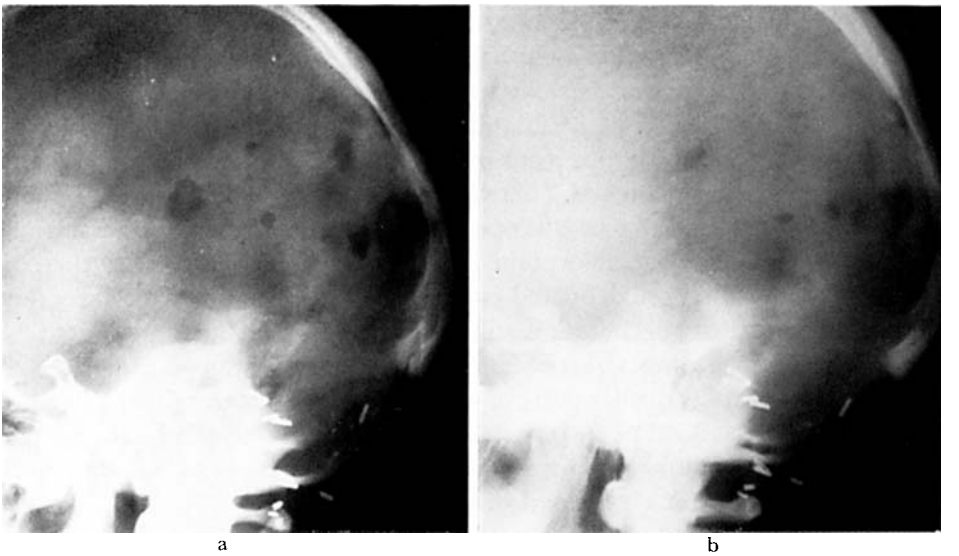


Fig. 9. Osteonecrosis in patient C (see Table 1). Portals and skin doses in R.

It is difficult to say anything definite about the relationship, if any, between the development of necrosis and the dose given, owing to the variation in the number of fields used and the duration of treatment. Radium or roentgen treatment has been given in previously published cases. The largest doses used were about 21 500 R in the course of 4 to 5 years (MIRIMOVA & ANDREENA 1962, and BROTSLAVSKIJ 1962) delivered with 160 to 180 kV roentgen. Superficial and deep therapy were used, with over 20 000 R/10 years as skin dose, in HAUBRICH & BREUER's (1958) patients. One of KOLÁR & VRABEC's patients received superficial therapy by the Chaoul method with 8 900 R. In other cases on record the dose ranged from 1 100 to 7 100 R. An attempt was made to form an opinion between the dose given and the development of osteonecrosis (see Table 1). Total skin doses between 3 000 and 4 500, and cumulative doses between 900 R and 1 600 R, given for 21 to 42 days, appeared to favour the development of necrosis, although it sometimes occurred even when treatment was administered in two series for 63 to 105 days with skin doses between 3 200 and 4 000 R. The necrosis sometimes progressed and at other times regressed. No correlation was evident between the size of the dose and the course of the destruction in the present material. It is probable that the occurrence or non-occurrence of necrosis depends more on individual factors than on the actual size of the dose given, provided that overdosage can be excluded. Age at the time of treatment appears to be an important factor, and both of the two patients in whom the necrosis regressed were young (13 and 10 years) but only one had received a relatively small dose.

Pathogenesis. Histologic examinations of osteonecrotic lesions have been published by BALLI & BARBANTI-SILVA (1931), CAMP & MORETON (1945),



a b

c

Fig. 10. Same case as in fig. 9. a) Two years after end of roentgen treatment. Patchy, irregular decalcification in the areas treated. b) Six years later. Changes smaller and less distinct. c) Further two years later. Further regression.

KNITTEL (1955), KOLÁR & VRABEC (1957) and HAUBRICH & BREUER (1958). The osteoblasts and osteoclasts are markedly reduced in number and sometimes altogether absent. The trabeculae in the spongiosa and the haematopoietic parenchyma are replaced more or less by granulation tissue, which may be richly vascularised, spongy or more fibrous. The compact bone may be thickened. Stasis, thrombosis and fibrosis of the blood vessels are sometimes present.

Various explanations of the causal mechanism of osteonecrosis have been offered. According to EWING (1926), the arrangement of the blood vessels in bones in the narrow Haversian channels render the bones very sensitive to radiation. He observed that irradiation of bones produced vascular injury with the formation of sclerotic connective tissue in the marrow cavity and disappearance of the osteoblasts. ZÖLLNER (1941) stated that the osteoblasts and osteoclasts in irradiated bone disappeared and concluded that the normal equilibrium between bone resorption and new formation of bone is thereby disturbed. When the dose delivered is small, it is mainly the osteoclasts that are injured and then regeneration still appears possible. But our patient C, in whom the osteonecrosis regressed, had received as large a skin dose as 4 200 R; only one of the other patients had been given a larger dose. WIELAND (1956) and DAHL (1934, 1935) reported, like ZÖLLNER (1941), that osteocytes are radiosensitive. BADE & KÜNTSCHER (1939) irradiated the femoral neck in dogs and noted that even small doses (2 400 R/60 days), producing only partial epilation, had a severe effect on the skeleton with complete suppression of the capacity of injured bone to recover. DAHL (1934, 1935) made the same observation in young rats, and observed that growing osseous tissue is more radiosensitive than most other tissues.

Radiation treatment was followed by epilation in all the patients of the present series, by atrophy of the skin and pigmentation in seven (A, F, G, H, I, K and Q), and by marked teleangiectasis in four patients (G, H, K and Q). Three patients, aged between 9 and 13 years (C, E and N), in whom necrosis had been detected one year after treatment, had no skin atrophy, pigmentation or teleangiectasis. These patients, like the animals in the experiments, were young, i. e. in a period of life when bony tissue may be more radiosensitive than the skin, as known from the inhibition of growth observed on irradiation of the epiphyses of long bones. In the light of these observations it is remarkable that none of the irradiated children presented evidence of any inhibition of growth of the cranium in the irradiated area. The balance between the resorption and new formation of bone thus appeared to have been relatively normal. This may be explained by the fact that these bones are membranous and not cartilaginous.

Surgical trauma. The site of the necrosis has often been the femoral neck, resulting in a fracture, in the cases of osteonecrosis reported. This may be explained by the already impaired circulation of this part of the skeleton in advanced age owing to obliteration of the acetabular artery. In analogy, changes in the calvarium might be expected to be situated in or near the bone flap. The changes proved most marked in the bone flap in three (O, R and N)

Table 2

Seven patients with irradiation sarcoma of the cranium

	Sex	Age at time of treatment in years	Dose	Interval in years between end of treatment and diagnosis of sarcoma	Site	Histologic type of sarcoma
Skolnik et coll. 1956	♂	16	Roentgen skin dose 6 050 R/41 days	3 1/2	Temporal	Osteosarcoma
	♀	1	Radium 9 600 mghrs 9 months	10	Frontal	Chondrosarcoma
Meredith et coll. 1960	♀	51	Roentgen skin dose 1 200 R/8 days	6	Temporal	Osteosarcoma
Raventos et coll. 1960	♀	27	Roentgen skin dose 2 100 R/45 days Maximal absorbed bone dose = 9 300 rad	17	Frontal	Fibrosarcoma
Wende 1962	♀	23	Roentgen skin dose 4 400 (?) R/4 years	17	Frontal	Fibrosarcoma
Present material Case 1	♀	7	Roentgen skin dose 3 000 R/35 days Maximal absorbed bone dose = 7 100 rad	6	Parietal	Fibrosarcoma
Present material Case 2	♀	25	Roentgen skin dose 2 900 to 3 850 R/40 days Maximal absorbed bone dose = 12 000 rad (hot spot)	5	Temporal	Fibrosarcoma

of the patients but considerable changes were also evident outside the flap (Fig. 8). In three of the patients (D, G and P) only diagnostic cerebral biopsy was done via a burr hole, in two (E and F), only a small craniotomy was performed, and one patient (M) was not subjected to operation (the histologic diagnosis in this case was obtained at autopsy) but clear-cut osteonecrosis was evident in bone not damaged by surgery. In several of the patients (Figs 9 and 10), the changes were situated far from the operation field. No definite relationship was thus evident between osteonecrosis and surgical trauma.

Sarcoma of the skull following irradiation. The five cases of sarcoma traced in the literature and the two described in this communication are summarized in

Table 2. These patients, one male and six females, were 1 to 51 years old at the time of treatment and 6 of them were under 30. Like the patients with uncomplicated necrosis, they were thus mainly young at the time of treatment. The predominance of females may be due to chance. The interval between the end of treatment and the clinical onset of the sarcoma varied between 3 1/2 years and 17 years, a range agreeing well with that observed for sarcoma due to irradiation in other parts of the skeleton, i. e. 1—24 years.

The skin doses, given to patients in whom osteosarcoma has later developed, range between 1 500 and 11 500 R (usually between 4 000 and 6 000 R). The patients with sarcoma of the calvarium had received skin doses ranging between 1 200 and 6 050 R. The calculated absorbed bone dose in the case of RAVENTOS et coll. (1960) was 9 300 rad and in the present cases 7 100 and 12 000 rad. The interval between treatment and the development of sarcoma does not appear to vary with the skin dose given.

The tumors often originated from previously diseased bone, usually tuberculous bone or bone affected by giant cell tumors in cases published of irradiation of sarcoma in bony tissue other than the cranium. It is noteworthy that in the present two cases the tumors were situated mainly in the bone flap, which in Case 1 appeared to have healed well, while in Case 2 considerable resorption had occurred along the line of the craniotomy. A sarcoma however had not developed in the region of any surgical defect in the cranium in any of the cases previously published.

According to JAFFE (1958), and ACKERMAN & SPJUT (1962), an irradiation sarcoma of bone is usually a fibrosarcoma, but sometimes the growths appear to be osteosarcomas or chondrosarcomas. The tumors in the 7 patients under discussion were fibrosarcoma in 4, osteosarcoma in 2 (including one with spicule formation (SKOLNIK et coll. 1956)) and chondrosarcoma in one patient. The question then arises as to whether the fibrosarcomas had developed from the bone or from irradiated soft tissue such as the galea or dura. A number of factors suggest that the growths had commenced in irradiated bone. First and foremost, the dose absorbed is largest in osseous tissue. Further, a clear relationship between the development of sarcoma and radiation necrosis was evident in several patients. In RAVENTO's (1960) case, roentgenography disclosed this radiation reaction 7 years before the appearance of the sarcoma, and in WENDE's (1962) case necrosis was verified histologically.

Case 2 of the present series had marked necrosis for nearly three years before the occurrence of the sarcoma and similar changes, though slight, were evident in association with the development of the sarcoma in Case 1. All the tumors grew extensively in the osseous tissue. In Case 1, in which this was demonstrated at operation, it was even more extensive than suggested by the roentgenograms

(in which evidence of a sarcoma was actually not strong). This widespread growth in the bone suggests that these fibrosarcomas are of osseous origin. The data on osteonecrosis are less reliable in the cases of osteosarcoma and chondrosarcoma neurocranii. MEREDITH et coll. (1960) considered it remarkable that a large osseous destruction beneath the tumor could not be demonstrated roentgenologically (roentgenograms not published). In the two patients of SKOLNIK et coll. the tumors were situated temporally and frontally near the base of the skull, which made it difficult to demonstrate necrosis, if present, radiographically.

CRUZ et coll. (1957) reported advanced osteonecrotic lesions in only two of 11 cases of irradiation sarcoma of bone outside the neurocranium, and they concluded that sarcoma may develop in bone moderately injured, while severely injured bone has not the capacity to react with neoplastic transformation. It is not known in our cases whether the radiation lesion from the pathologic point of view were true necrosis or radiation osteitis with atrophy of bone.

Complicated versus uncomplicated osteonecrosis. The diagnosis of osteonecrosis was made roentgenologically in the present cases, as in others on record. The changes are multiple, irregular, lytic and confined to the irradiated areas. The postoperative decalcification sometimes seen after craniotomy alone is of a clearly different appearance. The conditions to be considered in the differential diagnosis are infectious complication with osseous necrosis, growth of cerebral tumor per continuitatem, metastases or myeloma, and irradiation sarcoma. Apart from metastases from a medulloblastoma there is no reason to consider the possibility of bone metastases from malignant cerebral tumors. When infectious complications occur, they usually do so within a few months. One of our patients with radionecrosis, however, developed an abscess in the operation scar (he had bilateral osteonecrosis) 4 years after treatment, but none of the other patients had any signs of skin ulceration or osteitis.

Neurologic symptoms and signs, which occurred in most patients with osteonecrosis, could be ascribed to the basic disease or to changes in the brain due to the therapy (LINDGREN 1958). The soft tissue swelling was the initial symptom in the present two cases of radiosarcoma. It was also found that uncomplicated osteonecrosis progressed slowly during the first years and then became stationary or even regressed. Progression of roentgenologic changes more than five years after irradiation should thus suggest sarcoma. The roentgenologic changes may however, be very subtle.

Osteonecrosis alone is evidently of no clinical importance but when complicated by sarcoma the prognosis is not bright with rapid growth and often with

pulmonary metastases. The present two cases followed the same hopeless course as other cases of sarcoma of the cranium. The risk of sarcoma is small but it is one of the many factors that should be considered before deciding upon radiation treatment of intracranial tumors especially in young subjects.

SUMMARY

Radionecrosis of the skull in a material of 16 patients is described. The condition was more common after irradiation of children and young people, and the changes were not related to surgical trauma or the radiation dose delivered. A consideration of two patients with sarcoma of the skull indicated that soft tissue swelling or progression of cranial necrosis five years after irradiation or later should suggest a malignant change.

ZUSAMMENFASSUNG

Sechzehn Fälle von Radionekrose des Schädels werden beschrieben. Das Krankheitsbild war häufiger in Kindern und jungen Leuten; es hatte keinerlei Beziehungen zu Trauma oder zur Strahlendose. Zwei Fälle von Sarkom zeigten, dass Weichteilschwellung oder eine fortschreitende Nekrose fünf Jahre nach Bestrahlung Zeichen einer malignen Veränderung sind.

RÉSUMÉ

Description de la radionécrose du crâne sur 16 cas. Cette affection est plus fréquente après l'irradiation d'enfants et de jeunes, et les lésions sont sans rapport avec le traumatisme chirurgical ou la dose d'irradiation. L'étude de deux malades atteints de sarcome cranien montre que l'épaississement des parties molles ou la progression de la nécrose cranienne cinq ans ou plus après l'irradiation doit faire penser à une transformation maligne.

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