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Preface

The Third International Symposium is a continuation of our biennial meetings at the Orthopedic Department of the University of Basle. The aim is to discuss a well-defined and timely subject. Since 1965, our symposia have become an international tradition as can be seen from the active participation of colleagues from many countries. It is true that there are a few who always meet here, but one cannot deny a feeling of satisfaction and above all of sincere pleasure that this Symposium has grown from modest beginnings to its present size. At this meeting, 140 colleagues from 20 countries took an active part. We are proud, not because of the success of our own organization, but because a group of scientists from various countries have gotten together to pool their knowledge in a well-defined field. The fact that each participant can offer something to his fellows makes the journey to Basel worthwhile. In spite of our present means of communication, research and often its results are restricted to a narrow circle and consequently are not sufficiently known. This is particularly true of problems which are still under investigation. We are thankful that we could meet here to discuss a problem which is still unsolved. Perhaps, with the results of our discussions, we may help to alleviate the sufferings of others. The progress, whatever its outcome, is worth the endeavors of both participants and organizers. There is a basis for good results. The international character, esteem for the efforts of others and a careful comparison of one's own interpretation with that of others are the foundations of progress. Our Symposium has been held in an atmosphere of sincerity and mutual friendship. Let us hope that we have also achieved our goal this year. This wish applies not only to the academic problem but also to the improvement of social relations among colleagues and research workers. In this way, an exchange of opinions is possible and often more fruitful than an official discussion where prestige is often at stake.

We would like to thank the Georg Thieme Verlag for publishing this volume. Particular acknowledgement is due to the Government of the Canton of Baselstadt which, by presenting an enjoyable opening ceremony, aided personal contact such that the discussions took place in a very friendly atmosphere. The Firm Sandoz AG deserves our thanks for its generous support of our Symposium. We hope that this booklet with its summaries of papers and discussions will contribute to the aim of our meeting and that it will enjoy a corresponding circle of readers.

Basle, 1970

George Chapchal

Contents

I. Pathology, Diagnosis, Indication in Bone Tumors

Pathology of Bone Tumors

B. Engfeldt, Stockholm, Sweden

Primary bone tumors comprise a complex group and vary widely from one another in clinical presentation, biology and histology. Malignant and primary bone tumors are relatively uncommon. In the Swedish cancer registry they account for about 0.3—0.5 per cent of all cancers. It should be pointed out, however, that in this registry, tumors of the hematopoetic system are not included. When these cancers are included the incidence is about 2—3 per cent. However, bone is one of the tissues from which sarcomas most frequently arise. When looking at the age incidence it is also of interest to point out that in the case of primary malignant bone tumors there is a peak of high incidence of malignant tumors between 15 and 25 years of age while other types of cancers usually increase steadily with increasing age.

The etiology of bone tumors is unknown. Malignant bone tumors can be produced experimentally in various ways, for instance by ionizing radiation, by carcinogenic hydrocarbons and by beryllium and other metals. There is no evidence, however, that environmental factors are of importance in the production of spontaneous bone tumors in man.

There are certain conditions in bone which are known to be sometimes complicated with malignant changes, e. g., Paget's disease of bone which is supposed to be a precancerous condition, and certain benign cartilaginous lesions may also sometimes convert into malignant stages.

In Table 1 the incidences of some of the more common malignant primary bone tumors are tabulated. They cover a five-year period taken from the Swedish Cancer Registry. In this series osteosarcoma is the most common tumor and some idea of the relative frequencies can be obtained from the figures.

Table 1 Number of cancer cases of bone system by histological type and sex.

	Total	Males	Females
Osteosarcoma	121	61	60
Chondrosarcoma	91	53	38
Giant cell sarcoma	9	4	5
Ewing sarcoma	37	26	11
Fibrosarcoma	23	12	11
Angiosarcoma	2	—	2
Myxosarcoma	3	1	2
Adamantinoma, Teratoma	18	9	9
Sarcoma, unspec. and other	78	42	34
	382	208	172

Table 2 shows the sites of osteogenic sarcoma from this same material and it is evident that more than 50 per cent of these tumors arise in the lower limbs.

The classification of bone tumors has been widely discussed in recent years. Some of the entities have been recognized only recently, mainly by the work of such authorities as Jaffe and Lichtenstein.

The majority of bone tumors appear to arise from skeletal connective tissue and the tumors may comprise one or several of the more or less specifically differentiated components of connective tissue cells of bone. The tumors may show differentiation of bone, of cartilage, or of fibrous tissue. They

are histologically identified by the type of tissue dominating and the degree of differentiation. There are, however, also primary tumors of bone which take their origin from non-osseous components present in the skeleton, including the hematopoetic and lymphoreticular elements.

Table 2 Number of cases of osteosarcoma by location and sex.

	Total	Males	Females
Skull, face	6	3	3
Ribs, sternum and clavicle	5	2	3
Vertebral column	5	2	3
Upper limbs	17	6	11
Pelvic bones, sacrum and coccyx	9	6	3
Lower limbs	72	39	33
Multiple sites and site unspec.	7	3	4
	121	61	60

The histological grouping of tumors of bone is justified by the existing correlation between the histological structure and the biological properties of the tumors. The World Health Organization has a group of pathologists who are working on classification of bone tumors and a tentative scheme of this classification which Dr. Schajowicz has kindly made available to me is shown in Table 3.

Primary bone tumors may show a very complex pattern which could be well demonstrated in, for instance, cases of osteogenic sarcoma where you can find traces of more or less well differentiated skeletal components dominating in the different areas. You may find areas with chondroblastic differentiation, or areas where the production of more or less immature bone tissue is dominating, and you may have areas where the fibrous component dominates with the appearance of multinuclear tumor giant-cells (cf. Fig. 1a, b, c). There are good reasons for commenting briefly, in this connection, on giant cell tumor of bone, which also could vary considerably in terms of morphological features.

This tumor has a rather characteristic clinical appearance and x-ray findings. Sometimes, however, there are difficulties in interpreting the histology with respect to biological behavior. A few of these tumors

Table 3 Primary bone tumors.

	Malignant	Benign
Bone forming tumors	Osteosarcoma Juxtacortical osteosarcoma	Osteoma Osteoma osteoid Benign osteoblastoma
Cartilage forming tumors	Chondrosarcoma	Chondroma Osteochondroma Chondroblastoma Chondromyxoid Fibroma
	Giant — cell tumor (osteoclastoma)	
Marrow tumors	Ewing's sarcoma Primary reticulum-cell sarcoma of bone Primary lymphosarcoma of bone Myeloma multiple, solitary	
Vascular and connective tissue tumors	Hemangioendothelioma Hemangiosarcoma Hemangiopericytoma	Hemangioma Lymphangioma Glomangioma
	Fibrosarcoma Liposarcoma Malignant mesenchymoma Undifferentiated (pleomorphic) sarcoma.	Desmoplastic fibroma Lipoma
Dysembryonal tumors	Chordoma so-called "Adamantinoma" of long bones	

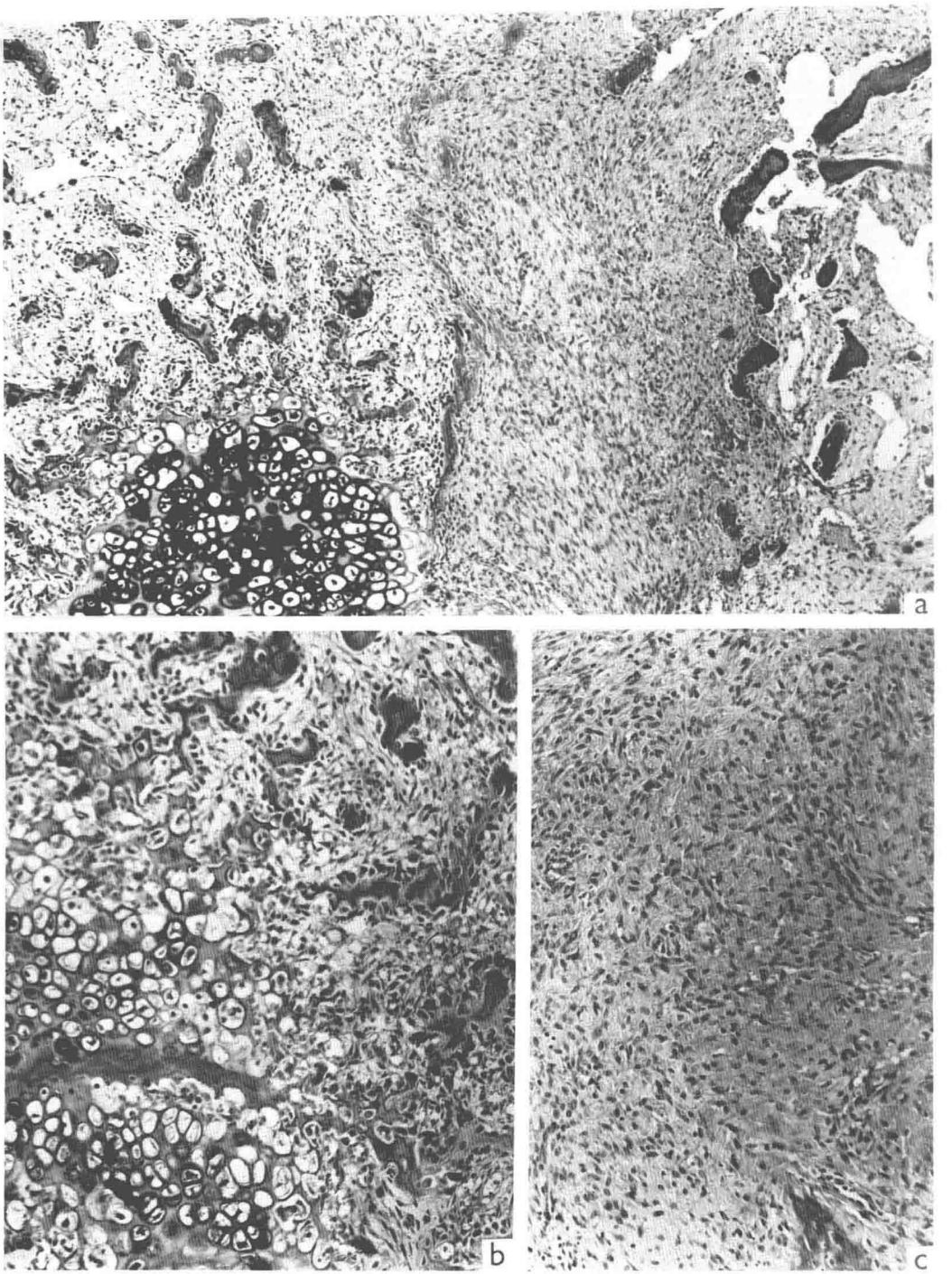

Fig. 1 a) Histologic section from a case of osteogenic sarcoma of the femur. H. and E. 150 x. b) Detail of the same tumor as shown in Fig. 1a, showing osteogenic and chondroblastic differentiation. 300 x. c) A fibrosarcomatous area of the same tumor. 300 x.

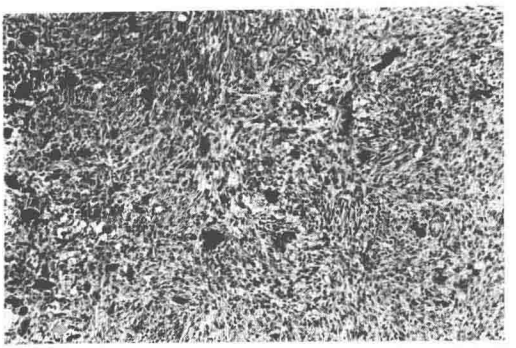

Fig. 2 Histologic section from a giant cell tumor of the tibia showing a cellular fibrous tissue with an abundance of multinuclear cells. H. and E. 300 x.

are clearly malignant. Most of them have a tendency to recur after curettage and when recurring they gradually become more destructive and may finally metastasize, most commonly to the lungs. An example of a tumor with a more uniform morphological picture is given by the Ewing sarcoma which is supposed to arise from primitive mesenchymal cells (Fig. 3).

After this brief introduction to the pathology of bone tumors I would also like to say a few words on the diagnosis of these tumors from the standpoint of the pathologist.

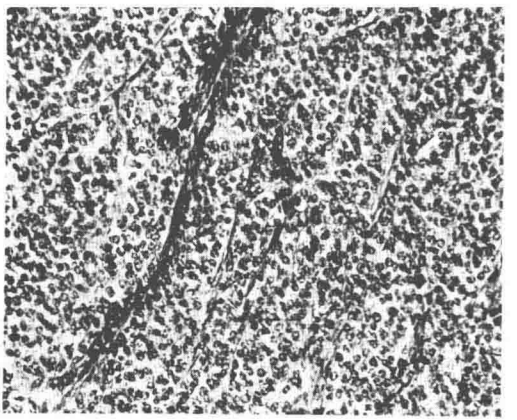

Fig. 3 Histologic section from a Ewing's sarcoma of the scapulae. Note fields of tumor cells with nuclei of fairly uniform appearance. H. and E. 300 x.

Biopsy before definite therapy is decided upon is considered an essential component of diagnostic clarification for lesions suspected of being bone tumors. Biopsy should be done in most cases and is certainly indicated in all cases where amputation or other radical surgery is planned. It should also be done, if possible, whenever radiation is to be the therapeutic procedure. It should be pointed out in this connection that it is essential for the pathologist to know that the tissue to be studied is representative and the selection of suitable areas for biopsy should be made with the cooperation of the surgeon, the radiologist and the pathologist.

Once a decision has been made to perform a biopsy, the question is how the material should be obtained. There are two major possibilies for obtaining material. There is the so-called closed biopsy — aspiration biopsy or needle biopsy — which has the advantage of constituting a limited intervention when compared with open or surgical biopsy. Opinion on the usefulness of these various methods differ among experienced pathologists. Lichtenstein, for example, is against needle biopsy while Schajowicz strongly favors this procedure. There is no doubt that needle biopsy has advantages in cases where it is possible to obtain material from sites such as a vertebra which would be very difficult to reach by open biopsy.

Needle biopsies also provide good diagnostic results in non-ossifying lesions of the marrow cavity such as reticular cell sarcoma or myeloma. In such cases the combination of the smear and histological embedding techniques applied on small aspirated tissue fragments usually leads to a correct diagnosis.

It seems, however, as if most of the orthopedic surgeons would prefer surgical biopsy, which could then be interpreted on frozen sections in cases where the tumor tissue consists only of soft tissue. If decalcification of the material has to be performed, paraffin embedded sections have to be studied. In

most cases, however, areas can be selected for biopsy which do not contain mineralized tissue, and in this way a rapid histologic diagnosis by frozen sections can be achieved. According to Dahlin, in at least 90 per cent of bone tumors there are soft areas that could be sectioned and examined for immediate diagnosis. When dealing with tumors composed of cartilage, however, paraffin section is, in general, to be recommended because this procedure provides a better basis than frozen sections for evaluating important cellular details with respect to benignancy or malignancy.

Finally, it should be re-emphasized that an accurate diagnosis of a bone tumor will be best achieved by close cooperation between the clinician, the radiologist and the pathologist.

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Discussion

In the lecture the author mentioned that giant-cell tumors often relapse, may become malignant and even metastasize.

But, in the Table 1, the 3d line, we have seen only "giant-cell sarcomas". I would like to ask how many of these sarcomas were primarly malignant and how many became malignant secondarily and after what period of time?

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The Significance of Angiography in the Operative Indication for the Treatment of Bone Tumors

E. Hipp, Dortmund, FRG

The treatment of bone tumors in general and the operative treatment in particular have undergone a change due to more recent findings and improvement in operative technique. In contrast to previous times, the question of diagnosis, particularly in relation to treatment by resection, has become a question of extreme importance.

Before one decides on a *biopsy*, all diagnostic measures which could reveal information concerning localization, extent and type of growth must be exhausted. In this connection, exact clinical evaluation including anamnesis as well as a thorough radiological examination should be emphasized including the use of radio-active isotopes, especially Sr^{85}.

As in the diagnosis of tumors in general (neorosurgery, surgery, urology) tumor angiography is well established in many Orthopedic Departments. The results of Ribbert (1903), which showed that the formation of new vessels in tumors is atypical, are regarded as the basis of angiography (Fig. 1a, b.).

From a technical standpoint, the flow of the contrast fluid must be registered serially, i. e. the arterial, capillary and venous phases must be recorded.

The evaluation of angiograms of bone is often complicated by a disturbing overlap

between bone and vessels. Consequently, the significance of vascular formation is often fraught with problems. In special cases, the *subtraction method* should be used.

The demonstration of tumor vessels in x-ray pictures allows decisive insight into the position and extent of the tumor and the type of growth, so that important indications for the final diagnosis, therapeutic procedure and prognosis are obtained. Changes in the angiogram are due to the fact that the normal vessels are displaced, markedly swollen or run atypically and that newly formed vessels can be demonstrated. The type of vascular formation of a tumor is an important indication of the type of growth.

In general, malignant tumors show an increase in the blood flow in serial angiograms, partly through the vessels which are normally placed but swollen, and partly through the newly formed vessels. In addition, the main artery of a tumor is displaced or tangled up by its branches.

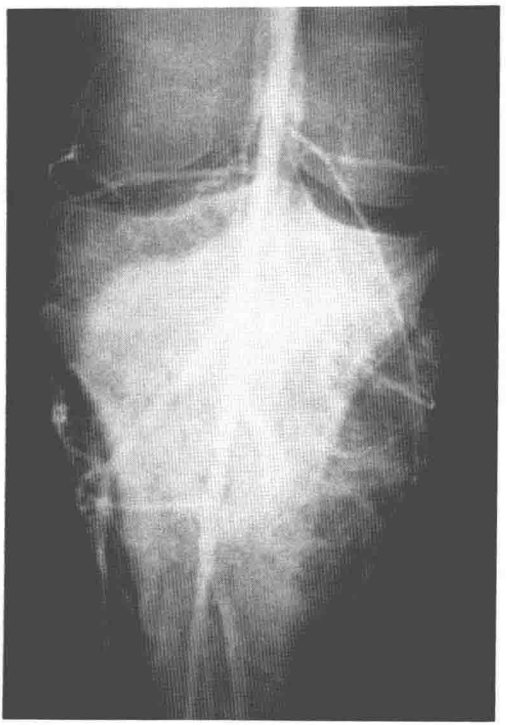

Fig. 1a Typical vascular formation in an osteosarcoma of the tibial metaphysis.

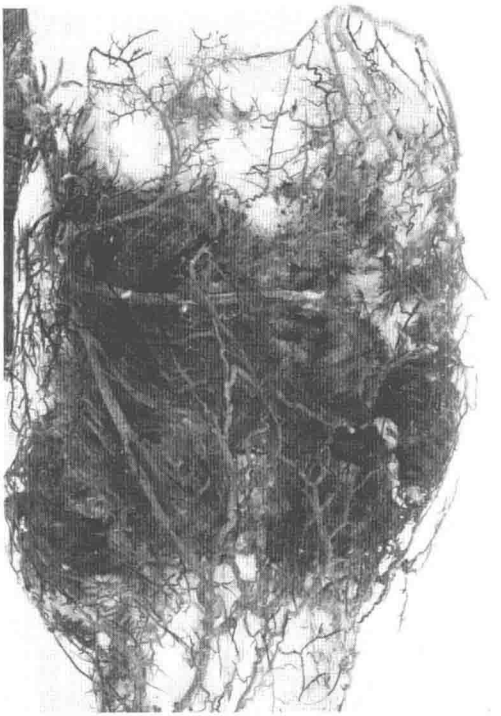

Fig. 1b Corrosion preparation of the tumor vessels.

The tumor vessels show varied forms. The diameter is often constant over a considerable length so that they look like a tube. It is often impossible to distinguish between arteries and veins. The walls of the vessels often show restricted dilatations which are the so-called blood pools. The flow of the contrast medium in the vessels of the tumor is irregular; it is sometimes increased and sometimes slowed up.

Even in the early arterial circulation phase, dilated vessels leading away from the tumor can be demonstrated. The contrast fluid often remains in the tumor vessels, particularly in the blood pools.

A variety of vascular types can be found in malignant tumors.

Pathological vessels in a tumor can be distinguished by their number, course and functional properties.

There are uniformly vascularized tumors, but the vascularization can also vary from one part of the tumor to another. One sees areas containing fewer vessels and others with extensive pathological vascularization. In marked bone-forming para-ossal osteosarcomas, the formation of tumor vessels may be slight. In addition, the demonstration of tumor vascularization can present technical difficulties. Therefore the subtraction method, mentioned above, must be used in these cases without fail.

The arrangement of newly formed vessels can be regularly spread over the entire tumor (net, ball or fan forms) or be irregular.

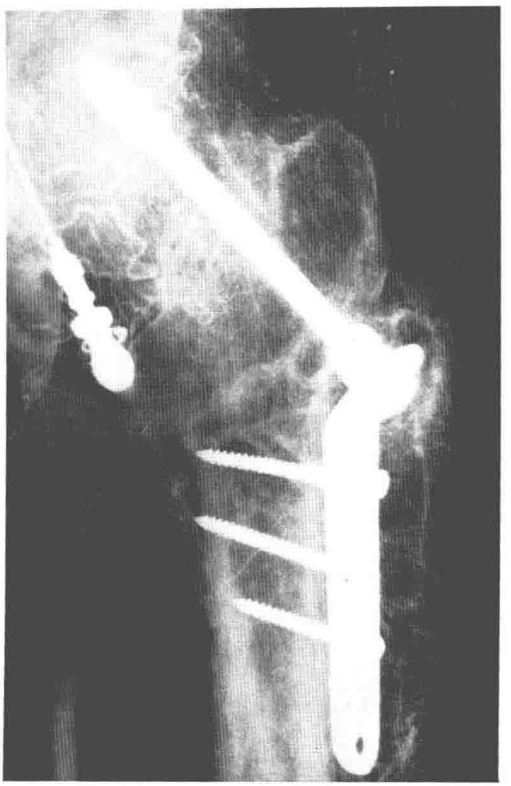

Fig. 2 Abnormal vascularization in granulation tissue (corrosion). Confusion with vascularization of tumor tissue.

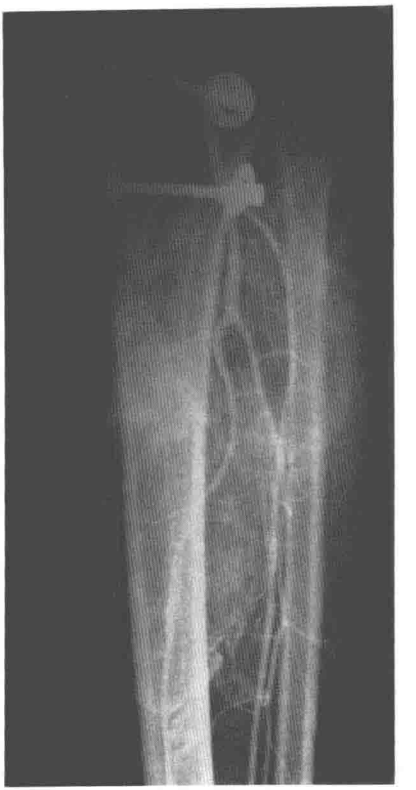

Fig. 3 Tumor vascularization in the area of a local recurrence of an osteosarcoma following treatment by resection.

The following general rule applies to the relation between vascularization and type of growth:

Richly vascularized tumors generally indicate marked malignancy.

Naturally, particular care must be taken in cases of abnormal vascularization which are found particularly in inflamatory processes (T. B., osteomyelitis) and in various granulation tissues, e. g. in metallosis. This type of vascularization can, however, be distinguished from tumor vascularization on detailed examination (Fig. 2).

What is the basic significance of angiography in the operative indication of bone tumors?

The vascular picture, including a complete record of all circulatory phases, often per-

mits exact *localization of a tumor* (intra- and extra-osseal) and of its borders, which is of extreme importance for evaluation of possible treatment by resection.

Preoperatively, decisive indications concerning the *properties of the growth* can be obtained if the position, type and extension of the vascular formation is analyzed. Numerous tumors show relatively similar vascular formations (osteosarcoma, in the region of the tibial tuberosity). Naturally, vascularization of an osteoclastoma, which according to Lichtenstein can be extensive even in the Grade I stage, must be considered.

With regard to a *biopsy*, it is necessary to distinguish areas of the tumor which differ in vascularization.

The extent of vascularization is related to the type of growth. This is important when distinguishing between benign tumors and say, tumor-like lesions.

Decisive results can be obtained from the follow-up controls or when a recurrence is suspected (Fig. 3).

Thus, as a diagnostic procedure, angiography is a decisive, specific radiological technique which, together with other diagnostic methods, can yield important details in the recognition and further evaluation of a tumor. However it must be performed to technical perfection and the findings must be correctly evaluated.

The Possibilities of Peripheral Arteriography and the Significance of Intra-osseus Angiography in the Indication for Operative Treatment of Bone Tumors

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Angiography is an important diagnostic aid in the differentiation between benign and malignant tumors. The angiographic symptomatology of malignant soft tissue tumors is also applicable to bone tumors. Mucchi et al. (1966) interpret the combination of vascular morphological changes in angiograms as pathognomonic for certain bone lesions and even emphasize an absolute agreement between angiographic malignancy and pathologic-anatomical malignancy.

The general criteria for nonmalignancy of bone tumors in angiograms are: no abnormalities of the arterial system or merely dislocations; curves or variations in diameter; and diffuse staining of the tumors with contrast medium (2, 9, 10, 22, 33). The signs for malignancy of bone tumors in angiograms are: considerable growth of arterioles around the tumor with abnormal, irregular course; cuff-like and convoluted pattern of arterioles; considerable variation in diameter; blood pools or so-called tumor lakes; prolonged staining by contrast medium beyond the arterial phase; and premature filling of veins (9, 11, 17, 18, 22, 26, 33).

The signs of vascular malignancy have been observed almost exclusively in bone tumors which have been expanding rapidly and have broken through the cortex and partly penetrated deep into the soft tissues. Therefore, the specific tumor vessels have found a connection to the peripheral vessels of the soft tissue. A radiological visualization by injection of contrast medium into overlying arteries is possible.

Are the angiographical signs of malignancy also valid for malignant tumors whose ex-