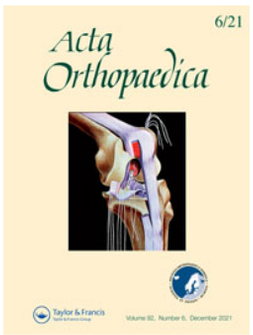

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ANGIOGRAPHY IN TUMORS OF THE EXTREMITIES

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Angiography in tumors of the extremities has been employed since 1929 when Dos Santos & J. Caldan reported their primary experiences. In 1950, these same authors described the angiographic characteristics of various disorders of the extremities. These were later confirmed and extended by other authors, especially Strickland (1959). On the basis of the current literature, it is possible to establish certain criteria upon which, in the majority of cases, it is possible to differentiate between malignant and benign processes. The signs of malignancy comprise:

1. *Pathological arteries,* i.e. newly formed, randomly distributed, cylindrical or uneven vessels, sometimes of varying diameter. These often display a more or less ordered pattern, resembling a net, paint-, or toothbrush. Some arteries end abruptly, others lead into lacunae (Figure 1).

2. *Pooling,* i.e. irregular, larger or smaller concentrations of contrast medium, resembling pronounced vascular dilatations or non-endothelial-covered, interstitial pools of blood in necrotic tumor tissue (Figure 1).

3. *Shunts,* which are defined as very rapid filling of veins because of almost direct arterio-venous connections (Figure 2).

4. *Veins* extending transversally over the surface of the tumor (Figure 2).

Phenomena such as hyperemia, simple vascular dislocation, and accumulation of contrast medium (flushing) may be seen in both benign and malignant tumors (Strickland 1959, Lindbom et al. 1960). Hypervascularization with pooling and shunt may be seen in benign

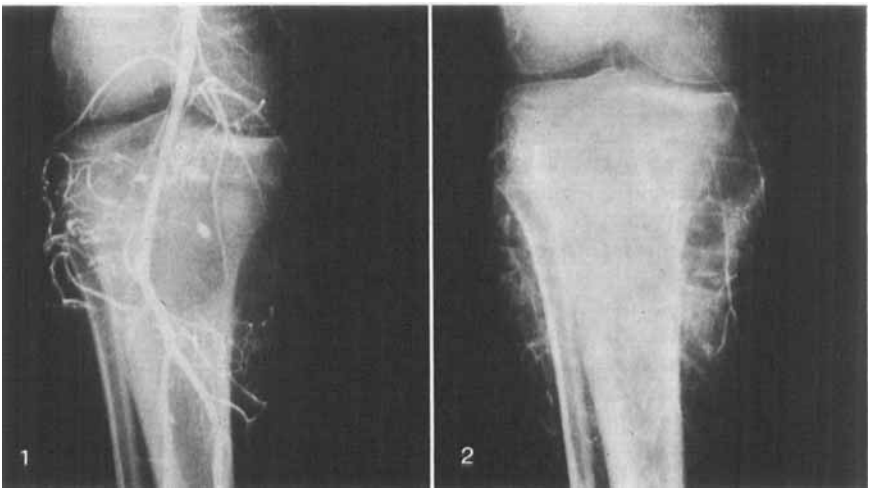

Figure 1. Osteosarcoma in an early phase of angiography with numerous pathological arteries, some of which end abruptly, and with characteristic pooling.
Figure 2. Osteosarcoma in a late phase of angiography, demonstrating rapid venous filling (shunt) and large veins extending transversally over the surface of the tumor.

processes such as hemangioma (Cockshott & Evans 1964, Rösch 1964), inflammation (Cockshott & Evans 1964, Lagergren et al. 1958), and organized hematoma (Stener & Wickbom 1966). With a single exception (Cockshott & Evans 1964), pathological, newly formed vessels have only been described with malignant tumors. Lagergren et al. (1960, 1961 a, b, 1962), in particular, have shown a high correlation between the degree of vascularization and malignancy. These authors, and others (Diethelm et al. 1969, Mucchi et al. 1960, Rösch 1964), emphasize that more precise identification is not possible with angiography.

Most authors regard angiography as a valuable supplement to other methods of investigation. It allows differential diagnosis between malignant and benign tumors, it provides a relatively precise indication of the size of the tumor, it suggests the optimal site for biopsy, and, finally, it provides guidance in operative intervention (Rosenberg 1964).

The aim of the present work has been to assess the accuracy of differential diagnosis and to evaluate the practical value of angiography in tumors of the extremities.

MATERIAL AND METHODS

The material comprised 84 patients with tumors of the extremities referred to the Department of Orthopedic Surgery, University Hospital, Copenhagen. Patients were selected on the basis of whether in the preceding five-year period a reasonably successful angiography had been obtained. (Three patients were excluded from the study because of inadequate angiographs; three others because their angiograms were missing at the second follow-up.) All cases had been histologically verified, often by several pathologists, as is customary with bone tumors, which, as is well known, often present major difficulties in diagnosis even for pathologists. Angiography was carried out seriographically in the conventional manner in two planes with the contrast medium injected as close to the tumor as possible. The angiograms were assessed twice; the second time by two of the present authors who made an independent examination of all pictures without knowledge of the original roentgenological description or of the histological diagnosis. The angiographs were graded only as to whether the pathological changes were benign or malignant; The assessments of the angiograms were ultimately compared with the original roentgenological descriptions in the case histories.

RESULTS

The material was distributed according to age and sex as shown in Table 1. The youngest patient was 8 years old, the oldest 72 years of age.

Table 1. Age (in years) and sex of the investigated material.

	0–20	20–40	40–60	Over 60	Total
Women	5	7	11	13	36
Men	18	8	13	9	48

Table 2. Angiographic diagnosis of malignant osseous processes.

	No.	Malignant	Benign	Normal
Osteosarcoma	17	17		
Parosteal osteosarcoma	1		1	
Ewing's sarcoma	3	2	1	
Chondrosarcoma	5	5		
Malignant osteoclastoma	2	2		
Fibrosarcoma	1	1		
Reticulosarcoma	1	1		
Metastases	4	4		
Total	34	32	2	0

The material was classified according to benign or malignant processes in the bones and soft tissues, respectively, as may be seen in Tables 2–5.

Table 2 shows that all osteosarcomas were correctly diagnosed whereas a parosteal sarcoma was erroneously judged to be benign (a false negative).

This was a 5 × 12 cm, solid, osseous, avascular tumor which had previously been treated radiologically.

One of the 3 Ewing's sarcomas was erroneously assessed as benign.

This was a 3 × 4 cm, solid, immobile tumor at the site at which, 5 years previously, a tumor had been extirpated and radiologically treated.

All other malignant bone tumors were correctly identified.

Table 3. Angiographic diagnosis of benign osseous processes.

	No.	Malignant	Benign	Normal
Simple cyst	2		2	
Aneurysmal cyst	2		2	
Osteoclastoma	1		1	
Osteitis	4		4	
Periosteitis	1			1
Incomplete fracture	2		2	
Total	12	0	11	1

Table 3 shows that none of the benign bone processes was erroneously judged to be malignant.

Table 4 indicates that two of the fibrosarcomas, the most frequent tumor of the group, were incorrectly assessed.

One, which was judged to be benign, was a 17 × 22 cm tumor at the site of a former tumor in the femural adductor muscles. An extirpation had been performed 3 years previously, followed by radiological treatment.

The other case involved a 2.5 × 5 × 5 cm, sharply defined tumor lying subcutaneously in the trigonum scarpae. On 3 previous occasions, a tumor had been extirpated at this site.

One of the four rhabdomyosarcomas was judged to be benign.

This was a 3 × 9 × 10 cm tumor, situated proximally in the left femural adductor muscles close to the vessels. There had been no previous operation or

radiologic treatment in this area, but the angiography was not technically optimal.

One reticulosarcoma was graded as benign.

This was a 4 × 11 cm, highly malignant tumor of the forearm which had received neither operative nor radiologic treatment previously. The angiography was performed as an aorto-cervical angiography, as the subclavian artery could not be catheterized.

Table 4. Angiographic diagnosis of malignant soft tissue processes.

	No.	Malignant	Benign	Normal
Fibrosarcoma	15	13	1	1
Rhabdomyosarcoma	4	3	1	
Neurogenic tumors	5	5		
Reticulosarcoma	1		1	
Liposarcoma	1	1		
Synovialoma	1	1		
Undiff. anaplastic tumors	2	2		
Total	29	25	3	1

Table 5 indicates that all of the benign soft tissue processes were correctly assessed on the angiograms.

Table 5. Angiographic diagnosis of benign soft tissue processes.

	No.	Malignant	Benign	Normal
Baker's cyst	3		2	1
Hemangioma	1		1	
Myxoma	2		2	
Muscular hernia	1		1	
Hematoma	2		2	
Total	9	0	8	1

Comparison with the original roentgenological descriptions showed that the primary diagnosis in 20 cases was incorrect, in 7 of these in spite of the fact that details were accurately described. These 7 were all correctly described as malignant at the second control of the pictures. For the remaining 13 cases, for which the angiographic diagnosis deviated even more from the correct assessment of the cases, 9 were

correctly described and 4 erroneously graded at the second control. In two cases of fibrosarcoma, the first assessment was correct, but the second was erroneous.

DISCUSSION

Like other authors, we have found a good correlation between angiographic and histologic diagnoses of malignancy. Angiographic assessment was most accurate for the often highly vascularized osteosarcomas. Hipp (1968) and Scholz (1953) believe that angiography renders pre-operative biopsy unnecessary. At present, we do not fully agree. However, this study and other investigations (Leroux & Delvigne 1967, Strickland 1959) support such an idea when the angiograms are definitely positive. Only a single false negative angiographic finding has been reported for osteosarcoma (Koskinen et al. 1968). Lagergren et al. (1961 a) state that sclerotic tumors are poorly vascularized and are thus difficult to assess. This is supported by our false negative diagnosis in a case of parosteal osteosarcoma.

The diagnosis of Ewing's sarcoma is difficult, whether by pathology or by angiography. Poppe (1969) has demonstrated that 20 of 59 Ewing's sarcomas could not be distinguished from osteomyelitis. Lagergren & Lindbom (1962) concur in this statement. Hipp (1968) and Dos Santos (1950) are of the opposite opinion and assert that Ewing's sarcomas always present pathological vessels within the tumor whereas osteomyelitis does not. Mucchi et al. (1966) are of the same opinion; they believe that tumor vessels always occur in Ewing's sarcoma and state that pathological arteries resembling a crumpled metal wire are especially characteristic (Figure 3). Our material is too small to contribute to this discussion, although we have noted "crumpled metal wires" in osteitis and eosinophilic granuloma.

Osteoclastomas may often present difficulties in angiographic diagnosis, as the more active forms may resemble malignant tumors (Strickland 1959, Mucchi et al. 1966). In our material, erroneous grading of this type of tumor occurred only at the first inspection.

Fibrosarcomas fall into two groups, those which are richly and those which are poorly vascularized (Lagergren et al. 1960). The latter may lead to a false negative diagnosis as happened in two of our cases.

Rhabdomyosarcomas are often highly vascularized (Lagergren & Lindbom 1962) and were therefore generally correctly identified on angiographs in our material, as was the case in the investigation by

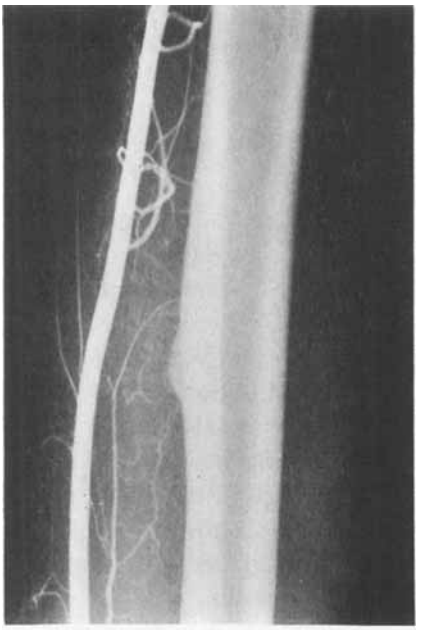

Figure 3. An almost avascular Ewing's sarcoma with some arteries resembling crumpled metal wire.

Rosenberg (1964). Our material offered a single exception to this, however, in that one rhabdomyosarcoma was definitely avascular and was thus misinterpreted. This tumor had not previously been subjected to either operation or radiologic treatment.

Reticulosarcomas are most often graded correctly (Diethelm et al. 1969). In our material there was a single false negative diagnosis in this group. Strickland (1959) also found a single false negative assessment in his investigation, but in his case radiologic treatment had preceded angiography.

Thus we found a total of 6 false negative diagnoses, of which 3 tumors had previously received radiologic treatment. Radiologic treatment is, as has been shown by Strickland (1959) and Breit (1969), of major influence for angiography in that the blood vessels in and near the tumor are altered and become unrecognizable, especially if the tumor is radiosensitive. Two of the radiologically treated cases were also surgically treated. One tumor was a regrowth on the site from which tumors had been extirpated several times previously. In 2 cases, there were regularly false negative assessments of tumors which are normally highly vascularized. It should, however, be noted that neither of the angiograms was technically satisfactory.

There were no false positive findings. Diethelm et al. (1969) have reported one case in which a histologically benign chondromyxoid fibroma appeared to be malignant by angiography. Staple et al. (1968) have reported on one case in which ordinary X-ray photographs and biopsy indicated an aneurysmal bone cyst whereas angiography suggested malignancy, and a subsequent new biopsy, taken on the basis of the angiographic findings, demonstrated malignancy. False positives are thus rare and should, when they appear, be taken as an indication of the need for re-biopsy guided by the angiographic picture.

It is thus our experience, like that of other authors, that only genuinely pathologically formed arteries may be taken as a definite indication of malignancy. We have found transversal veins, which are regarded as almost pathognomic by Strickland (1959), in an aneurysmal bone cyst, and Staple et al. (1968) also describe extensive formation of veins in this type of tumor as well as in giant cell tumor and osteitis fibrosa.

CONCLUSIONS

We, like many other authors, conclude that angiography of bone and soft tissue tumors is, according to the above criteria and when assessed by experienced radiologists, a reliable guide when it demonstrates malignancy, whereas indications of benignity on an angiogram do not exclude the possibility of a malignant tumor. As a rule, angiography gives an excellent picture of the extent of the tumor, which is often larger than might be expected from clinical investigations and ordinary roentgenograms. Angiography may thus be used as an operative guide in making biopsies, for the excision of soft tissue tumors, and in the preparation for necessary surgical intervention.

Angiography is a valuable supplement to other methods of investigation. In the case of the highly vascularized, rapidly growing, highly malignant sarcoma, convincing findings of malignancy on the angiograph may promote earlier operative intervention by eliminating the necessity of pre-operative biopsy.

SUMMARY

After a short survey of the literature to establish the angiographic criteria of malignancy (pathological arteries, pooling, shunt, extended veins), a material of 84 patients is presented. All patients were angiographed and all diagnoses were histologically verified. Good agreement

was found between the histologic and the angiographic diagnosis in deciding between malignancy and benignancy. The diagnoses of osteosarcomas showed the greatest accuracy. In six cases, angiography gave false negative findings: in one case after previous radiologic treatment, in two cases after combined surgical extirpation and radiologic treatment, and in one case after repeated extirpations; whereas in two cases the false negative findings could only be explained by technically inadequate angiograms. It is concluded that a positive angiogram is reliable for the diagnosis of malignancy, but less reliable if the angiogram indicates a benign tumor or no changes. In addition, angiography has in many cases offered excellent guidance for operative intervention.

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