

Histological grading of malignancy



The grading of soft tissue and bone sarcomas is important because of the prognostic impact and should be stated in the histopathological report (1-3). The clinical course of sarcomas varies within a particular histopathological entity. There is no generally accepted grading system for sarcomas (4) and there is an ongoing discussion which grading system to prefer. The French Federation of Cancer Centers system has been tested in several studies and is probably the best documented system, see table (5) (6) (7). Because there are so many histological types of sarcomas and subgroups therein it is difficult to validate a grading systems for sarcomas. The morphologic variables are of varying importance for the different types of sarcomas (8). Ideally there should be one specific grading system for every subtype of sarcoma, but that is not clinically meaningful.

In the SSG the histological grading of sarcomas has been based on a four-tired grading system primarily based on Broders grading model (9-11). Generally only untreated primary sarcomas using good quality slides and representative tissue are assessable for grading. Grade 1 and 2 means low grade malignancy and grade 3 and 4 tumors are regarded as high-grade malignant sarcomas. This system considers the degree of cellularity, cell and nuclear polymorphism, differentiation, the presence and amount of necrosis, haemorrhages, mitotic activity and growth pattern, but does not score the different parameters (12).

For many soft tissue sarcomas the grade is given from the histological diagnosis. For instance atypical fibroxanthoma of skin, dermatofibrosarcoma protuberans and well differentiated liposarcoma are all grade 1 sarcomas. Typical examples of grade 2 sarcomas include myxoid liposarcoma and many subcutaneous myxofibrosarcomas. For high grade sarcomas (grades 3 and 4) the grade is partly based upon histogenetic diagnosis and partly upon the morphologic features. Examples of grade 4 sarcomas include round cell liposarcoma and pleomorphic liposarcoma. Immunostains for evaluating proliferative activity with Ki-67 (MIB1) is also helpful (13, 14).

For myxofibrosarcoma a set of grading is described by Angervall and Kindblom (15).

Relation to prognosis is shown in a paper about liposarcoma where the four-tired grading system was a significant prognostic factor for metastases in a multivariate analysis (16).

Multivariate analysis showed that high malignancy grade according to the four-tired grading system was the main risk factor for adverse outcome in nonvisceral soft tissue leiomyosarcoma (17).

A widely used system is the French grading system (FNCLCC). This is based on tumor differentiation, mitotic count and the amount of tumor necrosis (4, 5). The total score of each of these parameters gives the grade. Grade 2 and grade 3 are considered high-grade malignant tumors, see table.

The French grading system for reporting of soft tissue sarcoma			
Mitotic count			
Score	Mitoses per 10 HPF*		
1	0-9		
2	10-19		
3	≥20		
* A high power field (HPF) measures 0.1734 mm ² . Standardized HPF should be used (Area of a circle, A=π r ²)			
Tumor necrosis			
Score	Amount of necrosis		
0	No necrosis		
1	<50% tumor necrosis		
2	≥50% tumor necrosis		
Tumor differentiation			
Score	Differentiation		
1	Sarcomas closely resembling normal adult mesenchymal tissue (e.g. low grade leiomyosarcoma).		
2	Sarcomas for which histological typing is certain (e.g. myxoid liposarcoma, myxoid MFH [#])		
3	Embryonal and undifferentiated sarcomas, sarcomas of doubtful type, synovial sarcoma, osteosarcoma, PNET**		
Diagnosis	Differentiation score		
Well-differentiated liposarcoma	1		
Well-differentiated fibrosarcoma	1		
Well-differentiated leiomyosarcoma	1		
Well-differentiated	1		

chondrosarcoma			
Myxoid liposarcoma	2		
Conventional fibrosarcoma	2		
Well-diff. malignant haemangiopericytoma	2		
Myxoid MFH*	2		
Typical storiform/pleomorphic MFH	2		
Conventional leiomyosarcoma	2		
Myxoid chondrosarcoma	2		
Conventional angiosarcoma	2		
Round cell liposarcoma	3		
Pleomorphic liposarcoma	3		
Dedifferentiated liposarcoma	3		
Poorly differentiated fibrosarcoma	3		
Conventional malignant haemangiopericytoma	3		
Giant cell and inflammatory MFH	3		
Poorly diff./epithelioid/pleomorphic leiomyosarcoma	3		
Synovial sarcoma	3		
Rhabdomyosarcoma	3		
Mesenchymal chondrosarcoma	3		
Extraskeletal osteosarcoma	3		
Extraskeletal Ewing's sarcoma/PNET**	3		
Alveolar soft part sarcoma	3		
Malignant rhabdoid tumor	3		
Undifferentiated sarcoma	3		
<p>Note: Grading of malignant nerve sheath peripheral tumor, embryonal and alveolar rhabdomyosarcoma, angiosarcoma, extraskeletal myxoid chondrosarcoma, clear cell sarcoma and epithelioid sarcoma is not recommended.</p> <p>#MFH, malignant fibrous histiocytom **PNET, primitive neuroectodermal tumor</p>			
Histological grade:			
Score	Grade		
2 or 3	1		
4 or 5	2		
6, 7 or 8	3		

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