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**Abstract Title:** Why Can't We All Speak The Same Language? An Analysis Of The Definition And Significance Of Margins In The EURAMOS-1 Trial

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**Background:**

The EURAMOS-1 trial registered 2,260 patients from 17 countries between 2005 and 2011 of whom 1,334 joined one of two postoperative randomisations. Surgery was at the discretion of the local team and followed neoadjuvant chemotherapy(CT). Following surgery, the pathologist assessed the margins achieved by the surgeon (Enneking classification) and the response to CT (good responders <10% viable tumour; poor  $\geq$ 10%)

**Questions / Purposes:**

This report documents the differences identified between different groups in the description of the margin achieved and the significance that had on the risk of local recurrence (LR). The aim is to try and clarify what (if any) is the importance of describing the margins of excision and whether there is a need for a new, universally agreed definition of margins

**Patients and methods:**

All eligible patients who underwent surgery and had assessment both of CT response, margins of excision and follow up were included in the study (n=1,952). The frequency of the reported margin of excision was identified, as was the incidence of LR, based on the four contributing groups (COSS, COG, EOI, SSG) – the groups are not attributed to the labels here and absolute numbers are presented to facilitate this

**Results:**

Huge variations were noted across the groups in the description of margins achieved. This could not be explained on the basis of the type of surgery carried out (Limb salvage vs amputation). The proportion with a wide or radical margin ranged from 55% in Group A to 95% in Group D but the incidence of amputation was similar across all groups (10%)

The relevance of these labels was explored by investigating the reported risk of LR by group and margin. For convenience, Groups A & B were combined (high reported incidence of marginal or worse margins) and Groups C & D were combined (together reported 94% of patients with wide or radical margins). Ignoring competing risks, the proportion of patients with LR for Groups A&B was 7.5% and for C&D was 6.6%.

Investigation of margins achieved and the risks of LR are presented in Table1, and the effect of preoperative CT was added in Table2

**Conclusions:**

The definition of margins and the relevance of these varies hugely between the four groups studied. In groups A&B, a definition of radical (which should mean compartmentectomy of all involved compartments) completely prevents LR whilst this is not achieved in Groups C&D. Most surgeons would agree that an 'adequate' margin is one that is either wide or radical. If that was the case, then Groups C&D, which have considerably higher rates of adequate margins (94%), would be expected to have much lower rates of LR. This is not apparent. Instead, groups A&B have worse reported margins but similar rates of LR. Interestingly, groups A&B had no reported difference in LR between marginal and wide margins. If however the CT response is added to the margin a more useful classification can be obtained.

The existing definition of margins is not fit for purpose. A new definition is needed for osteosarcoma that has true international credibility. This should include the effectiveness of CT which has been shown to have key importance in predicting the risk of LR.

**Table 1: Percentage of patients with surgical margin type (and amputation), by group**

Label applied to surgical margins	Group			
	A	B	C	D
Radical	9%	9%	6%	15%
Wide	46%	64%	87%	80%
Marginal	40%	22%	6%	4%
Intralesional	4%	3%	1%	1%
Not known	1%	2%	0	1%
% with wide/radical margin	55%	73%	93%	95%
% amputation	13%	11%	9%	12%

**Table 2: Percentage of patients with local recurrence**

Part A	Group		
Label applied to surgical margins	A&B	C&D	Total
Radical	0%	6.1%	4.4%
Wide	8.4%	6.0%	6.5%
Marginal	7.9%	14.7%	9.9%
Intralesional	11.1%	25.0%	15.4%
Not known	0%	9.1%	5.9%
<b>Total</b>	<b>7.5%</b>	<b>6.6%</b>	<b>6.8%</b>
Part B			
Label applied to surgical margins	A&B	C&D	Total
Radical	0.0%	6.1%	4.4%
Wide/Marginal with good necrosis	6.5%	4.6%	5.1%
Wide / Marginal with poor necrosis	10.5%	8.5%	9.4%
Intralesional	11.1%	25.0%	15.4%
<b>Total</b>	<b>7.5%</b>	<b>6.6%</b>	<b>6.8%</b>