Letter to the Editor

Evaluation of histological scoring systems for tissue-engineered, repaired and osteoarthritic cartilage

We highly appreciated the interest in and comments of Dr Longo and colleagues on our publication. We realize that we have not completely adequately used the term viability in the description of the modified Mankin score, referring to the tissue in general rather than to the cell population inside it. However, we do think that the parameter “cell viability” incorporated in the International Cartilage Repair Society (ICRS) paper1 and referring to the absence of “necrotic, and apoptotic cells” and “pycnotic nuclei” (hallmark of apoptosis) may still be useful in describing general tissue quality. To this end, being able to detect all stages of apoptosis may not be an absolute prerequisite. The number of apoptotic bodies, which can be easily visualized by light microscopy at higher magnification2, can be expected to directly correlate with the total amount of cells in different stages of apoptosis and hence this number may still be indicative of the extent of apoptosis occurring in the tissue, though the relation may not always be fully linear. Dedicated research experiments correlating straightforward histological staining with more specific stainings, for example for caspase-3, or for a somewhat later stage of apoptosis, DNA fragmentation, may shed a final light.

Finally, we are happy to have a chance to address an issue that has been attracting our attention lately. As Longo and coauthors mention, there seems to be increasing confusion in the field of regenerative medicine and tissue engineering about the terms apoptosis and necrosis.

From a cell biology perspective, which is where we are when discussing cell viability, these terms have been clearly defined and taught to (medical) biology students for several decades: necrosis and apoptosis are two separate processes, with a different cause, following different routes and having different consequences3. Necrosis is initiated by direct external trauma, such as hypoxia or toxins. Apoptosis is caused by intra- or extracellular signals and requires protein synthesis and adenosine triphosphate (ATP), whereas necrosis does not. In necrosis, membrane integrity is fully lost, leading to leakage of degrading proteases and in turn an inflammatory response, whereas apoptosis is never harmful to neighboring cells4. Of course, the final result for the cell is the same, i.e., death. However, we feel that definitions should be adhered to according to the fields of science they were generated in, rather than according to linguistic arguments. We hope to have cleared some of the confusion arising lately, thus facilitating scientific discussion and understanding.

Conflict of interest
None.

References


L.B. Creemers, M. Rutgers, D.B. Saris
Department of Orthopaedics, The Netherlands University Medical Center Utrecht,
* Address correspondence and reprint requests to: Daniel B. Saris, Department of Orthopaedics, University Medical Center Utrecht, Huispost G05.228, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.
Tel: 31-88-7556971; Fax: 31-302510638.
E-mail address: d.saris@umcutrecht.nl

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