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LETTER TO THE EDITOR

cR and pR: The Residual Tumor Classification Revisited

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Introduced by the American Joint Committee on Cancer (AJCC) in 1978 [1] and subsequently established in the 4th edition of the Tumor, Node, Metastasis (TNM) system the definition and interpretation of the R Classification has significantly changed over time. R describes residual tumor following antitumor therapies and thus reflects therapy effects. Every report on a tumor specimen should include a statement concerning the R status [2]. The intention of the initial R Classification was a feedback to the surgeon concerning the completeness of the resection [3, 4]. For specific entities, e.g. colorectal cancer [5], the R Classification was further developed into a prognostic parameter [2]. In the following years it was extended from the locoregional tumor to metastases, thus shifting its meaning to a systemic residual tumor burden following any primary therapy [6–9].

By definition two parts are essential for the establishment of the R status in a pathological report [2]:

1. Clinical evaluation of the local treatment success (usually not provided to the pathologist).
2. Histopathological assessment of the margins from the primary tumor, regional lymph nodes, or distant metastases.

The R Classification must be established by an individual who has access to the complete data (surgeons, oncologists, radiooncologists, tumor registrars, or pathologists) [2].

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Finally, the R Classification is nowadays even an important parameter in the context of quality assurances measures in certified cancer centers where surgeons need to stick to predefined quota to maintain their accreditation (for example www.onkozert.de/downloads/eb_lunge-F1(160714).pdf). In turn, pathologists need to provide the R Classification in their reports on malignant tumors to fulfill the quality assurance criteria as well. However, due to the refinement of the R Classification over time, the following issues arise:

- Surgeons expect a feedback on the local excision but get a feedback on systemic residual tumor.
- Pathologists have to report on systemic residual tumor although only local excision specimens are assessed.
- Oncologists may interpret R1/R2 as a local problem, which might significantly affect treatment decisions (e.g. radiation vs. systemic chemotherapy).

Indeed, in a recent national survey among experts of certified lung cancer centers [10] it became evident that there is a high heterogeneity in the application and interpretation of the R Classification. There is a significant heterogeneity in the margins routinely assessed, interpretation of the criteria for R0/R1/R2, and specifically if only the local tumor or the systemic view is considered the basis of the R status. More than 50% of the participants considered the current guidelines as not sufficient. Only the minority was aware of all R categories (e.g. Rx, R0, R0 < 1 mm, R0 > 1 mm, R0(un), R1(is), R1, R2, R2a, R2b, R2c) and no one is using all of them in daily routine. Specific categories like R(un) were considered as not meaningful by >90% of the participants. Furthermore, it became evident that pathologists and surgeons have a divergent view on the R Classification. Almost two thirds of the pathologists reported that they

get insufficient clinical information. In many centers pathologists solve the problems in the correct application of the R Classification by adding "local" to the R factor, which actually means that they stick to the initial definition from 1978.

Taken together, we have a delicate classification system with high prognostic potential and impact on treatment decisions, which is obviously not accepted by many and applied with high variability [11, 12].

How can one overcome these problems?

A first step to a generally accepted and reproducible R Classification in pathological reports would be that pathologists only have to judge on what they actually analyze – in analogy to the TNM system. Here, pathologists provide a pTNM classification in their reports based on the assessment of the resected specimens and clinicians can modify this by applying a cTNM classification under inclusion of systemic findings.

Therefore, it is suggested to refine R accordingly:

pR: Residual tumor status based on the assessment of resected specimens by the pathologist.

cR: Residual tumor status based on the local resection and systemic findings.

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