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Assessment of the tumor bed area in patients with breast cancer and RCB class I after neoadjuvant therapy: comparison of original and modified method

N. Amirov[1], N. Mikhaskova[2], P. Krivorotko[1], A. Kudaybergenova[2];
[1]Breast Tumor Department, [2]Pathology Department, NMRC of Oncology named after N.N. Petrov, Saint Petersburg, Russian Federation

Background

One of the important prognostic and predictive markers in the histological assessment of breast cancer (BC) after neoadjuvant therapy (NAT) is the Residual Cancer Burden (RCB) index. In the original formula developed by MD Anderson Cancer Center the linear dimensions of the tumor bed are taken into account, which makes it impossible to assess fragmented material, for example, when performing vacuum-assisted biopsy. Considering this limitation, an attempt was made to modernize the method for evaluating tumor response to NAT by recalculating the RCB index using the area of the tumor bed based on digital images (scans) of histological slides obtained from sectoral resections in patients with early-stage BC.

Methods and Materials

A single-center retrospective study included 20 patients with ypT1a-cN0 stage breast carcinoma who had undergone neoadjuvant systemic therapy (FAC-T — 3 patients, AC-T — 8, AC — 2, DHP — 1, T — 2, EC+D+TRAST — 1, TCARB — 1, TCHP — 2) and were classified as RCB class 1.

Digital scans of histological slides were obtained using the 3D HISTECH PANORAMIC 1000 scanner. Measurements of the tumor bed were carried out using two methods: traditional MD Anderson technique, which defines the tumor bed area with the assessment of the two largest dimensions of the tumor bed, and a modified in-house technique, which implies manual delineation of the entire area of tumor bed on the histological scans using a stylus within the 3D HISTECH SlideViewer 2.5.0 software. The measured areas were then used to recalculate the RCB index according to the original formula, which includes extracting the square root of the area.

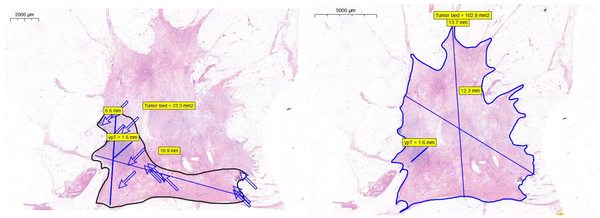


Figure 1. Residual breast tumor presented as a concentric nodule measuring 1.6 mm in its largest dimension. Blue arrows indicate isolated tumor cells within the tumor bed. **A.** Tumor bed boundaries delineated according to the standard RCB assessment method. **B.** Tumor bed boundaries delineated using the modified method.

Table 1. Clinical characteristics of included patients

Age, years; *mean (range)*	44.3 (22 – 60)
Maximum tumor size before NST, mm; *mean (range)*	30.3 (18 – 55)
Tumor area before NST, mm2; *mean (range)*	805.3 (252 – 1980)
Maximum tumor size after NST, mm; *mean (range)*	13.8 (5 – 24)
Tumor area after NST, mm2; *mean (range)*	155.3 (21 – 391)
TNM: cT	
cT1	1
cT2	15
cT3	**1**
cT4	3
TNM: cN	
cN0	7
cN1	10
cN2	2
cN3	3
Clinical Stage	
I	1
II	14
III	5
Type of surgery	
Breast-conserving surgery	13
Mastectomy	7

Results

The mean tumor bed area calculated using the MD Anderson method was 76.67 mm² (range: 14.2-258.7), whereas for the modified method, the mean was 153.65 mm² (range: 35.6-535). The mean RCB index for the standard method was 1.034 (range: 0.804-1.316), and for the modified method — 1.102 (range: 0.829-1.461). The obtained data was normally distributed in both groups.

A high correlation was found between the two methods, indicating a high consistency between the methods (Pearson's Correlation r = 0.96, p<0.001; Spearman's Correlation ρ = 0.95, p<0.001). The mean difference in RCB index between two methods was 0.068 (95% CI: +0.040 to +0.096).

Table 2. Pathologic assessment of the tumor bed

	Original method	Modified method
Mean tumor bed area, mm2	76.67 (14.2 – 258.7)	153.65 (35.6 – 535.0)
	RCB index	
Mean	1.034	1.102
Median	1.040	1.087
Interquartile range	0.272	0.277
Standard deviation	0.158	0.183
Confidence interval	[0.105; 0.212]	[0.121; 0.246]
Shapiro-Wilk test	0.940	0.943
P-value	0.242	0.270

Table 3. Correlation between original and modified methods

	Original method	Modified method
	Correlation	
Pearson correlation	r = 0.96	
Spearman correlation	p = 0.95	
Paired student t-test	t = 0.95 (p < 0.0001) (Modified – Original): + 0.068	

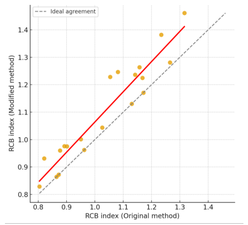


Figure 2. Scatter plot demonstrating the correlation between RCB index values obtained using the original and modified method. The solid red line indicates the linear regression fit.

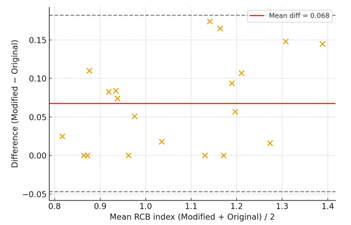


Figure 3. Bland–Altman plot showing the agreement between the modified and original RCB assessment methods. The red solid line denotes the mean difference (+0.068), indicating a consistent upward bias of the modified method.

Results *(continued)*

According to the t-test, the difference between the two methods was statistically significant (p < 0.01). The modified method demonstrated systematically higher values of RCB index. Moreover, when applying the modified method, 2 out of 20 patients (10%) were reclassified from RCB class 1 to RCB class 2.

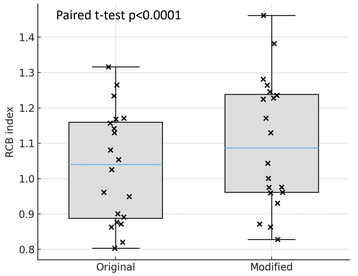


Figure 4. Distribution of RCB index values obtained with original and modified methods. Each marker represents an individual patient. Solid blue line represents median value.

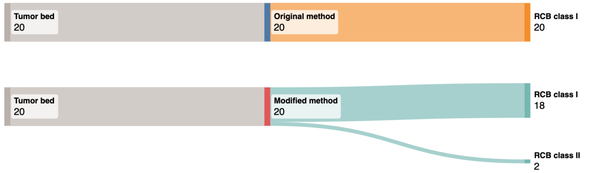


Figure 5. Sankey diagram showing reclassification of RCB classes using the modified method compared to the original method.

Conclusions

The proposed modified method of tumor bed assessment correlates highly with the classical approach in calculating the RCB index. Larger studies are needed to determine the clinical significance of a persistent slight overestimation of the RCB index using the modified method.

Contact

Nikolay Amirov
NMRC of Oncology named after N.N. Petrov, Saint Petersburg, Russian Federation
Email: amirovn17@gmail.com
Phone: +7 (953) 368-24-17

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