

## ULTRASOUND PREDICTORS FOR MALIGNANCY OF THYROID NODULES – “CALCIFICATIONS”

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### ABSTRACT

**Introduction:** The current clinical approach to diagnosis of thyroid nodules is based on the results of the ultrasound examination combined with data from fine-needle biopsy of the thyroid (FNAB). Ultrasound characteristics associated with malignancy have been widely discussed in scientific literature in order to early identify the risk nodules. Visualization of calcifications within the nodule often indicates an increased risk of malignancy. The prognostic value of different types of calcifications (microcalcifications, macrocalcifications and peripheral calcifications) differs significantly. **Objective:** To evaluate the prognostic significance of the ultrasound features - microcalcifications, macrocalcifications and peripheral calcifications for the risk of malignancy of thyroid nodules. **Patients and Methods:** 270 patients with thyroid nodules were included in the study, mean age  $48,89 \pm 0,77$  years; m:f = 1:11.86. An ultrasound evaluation and FNAB on a total of 329 nodules had been performed. Cytological evidence of malignancy was identified in 28 cases, the diagnosis differentiated thyroid cancer was confirmed histologically. **Results:** Microcalcifications were identified in 4.7% of benign and 25.0% of malignant nodules macrocalcifications - in 9.6% of benign and 25.0% malignant formations, peripheral calcification - in 3.7% of benign and 0.0% of malignant nodules. The analysis found that microcalcifications were statistically significant risk factor for malignancy (sensitivity - 25.00%; specificity - 95.35%; positive predictive value - 33.33%; negative predictive value - 93.18%). The presence of macrocalcifications was also recognized as a risk factor for malignancy (sensitivity - 25.00%; specificity - 90.37%; positive predictive value - 19.44%; negative predictive value - 92.83%). There were no significant differences in the incidence of peripheral calcifications in both malignant and benign nodules. **Conclusion:** The presence of microcalcifications and macrocalcifications indicate an increased risk of malignancy and should be taken into account in an integrated assessment of the risk profile of thyroid nodules. Peripheral calcifications are not significant factor for the prognosis of the risk of malignancy of thyroid nodular formations.

**Key words:** *thyroid nodules, ultrasound examination, calcifications*

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**Objective:** To evaluate the prognostic significance of the ultrasound features - microcalcifications, macrocalcifications and peripheral calcifications for the risk of malignancy of thyroid nodules.

**Patients and methods:** 270 patients with thyroid nodules were included in the study, mean age  $48,89 \pm 0,77$  years; m:f = 1:11.86 (tab. 1). An ultrasound evaluation and FNAB on a total of 329 nodules had been performed. Cytological evidence of malignancy was identified in 28 cases, the diagnosis of differentiated thyroid cancer was confirmed histologically

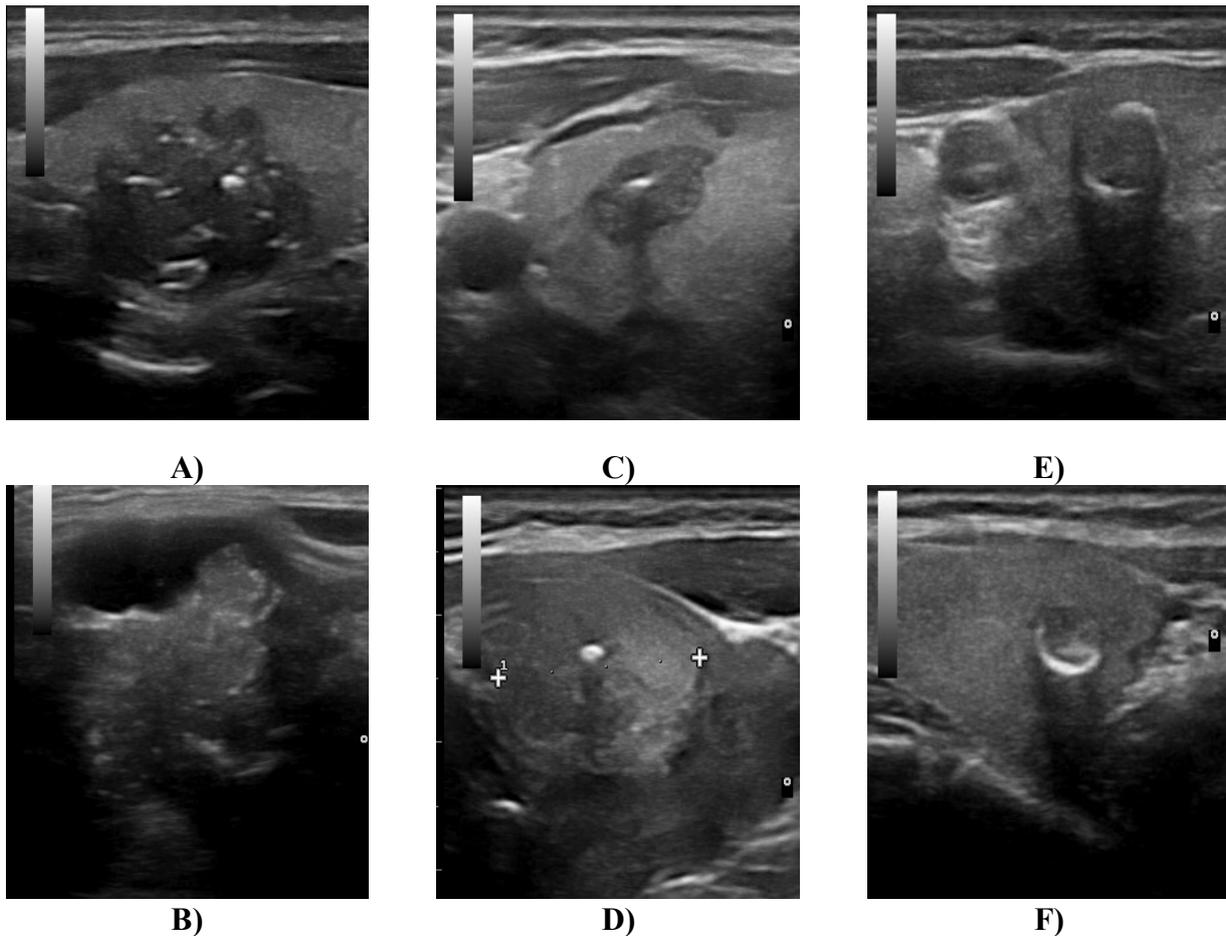
**Table 1.** Characteristics of the studied patients

		N	%
<b>Patients</b>	male	21	7,78%
	female	249	92,22%
	total	270	100%
<b>Age (years) Range</b>		48,89±0,77 (20-83)	
<b>Nodules</b>	solitary	160	48,63%
	multiple	169	51,37%
	total	329	100%
<b>Autoimmune thyroid disease</b>			
	yes	28	8,51%
	no	301	91,49%

**Results:** The analysis found that microcalcifications were a statistically significant risk factor for malignancy (sensitivity – 25.00 %; specificity – 95.35 %; positive predictive value – 33.33 %; negative predictive value – 93.18 %) (fig. 1A, 1B). The presence of macrocalcifications was also recognized as a risk factor for malignancy (sensitivity – 25.00 %; specificity – 90.37 %; positive predictive value – 19.44 %; negative predictive value – 92.83 %) (fig. 1C, 1D). There were no significant differences in the incidence of peripheral calcifications in both malignant and benign nodules (fig. 1E, 1F) (tab.2)

**Table 2.** Distribution of different types of calcifications found in benign and malignant thyroid nodules

		benign	malignant	OR [95%CI]	P
<b>Microcalcifications</b>	yes	14	7	6.833 [2.490-18.756]	=0.001
	no	287	21		
<b>Macrocalcifications</b>	yes	29	7	3.126 [1.225-7.981]	=0.022
	no	272	21		
<b>Peripheral calcifications</b>	yes	11	0	0.912 [0.881-0.944]	=0.608
	no	290	28		



**Figure 1.** A) and B) – microcalcifications; C) and D) – macrocalcifications; E) and F) – peripheral calcifications

**Discussion:** Ultrasound evidence of calcification may occur in up to 30% of thyroid nodules and are divided into macro-, micro- and peripheral calcifications. Microcalcifications are defined as small (<2 mm) dot-like hyperecho, usually without dorsal acoustic shadowing (1). They are considered to be aggregates of psamoma bodies and are highly specific predictor of malignancy. The analysis of our data confirms the importance of microcalcifications in assessing the risk of malignancy of thyroid nodules. Macrocalcifications (> 2 mm) have dorsal acoustic shadowing, and can be observed either in benign or malignant nodules. These dystrophic calcifications are found in areas of fibrosis, tissue degeneration and necrosis and are a common finding in long-standing benign nodes (4). According to some analysis the presence of macrocalcifications in solid thyroid formations increases the risk of malignancy compared with nodules without calcifications (2) which is also confirmed by our results. Peripheral calcification "egg shell" type have long been considered indicators of benign nature of thyroid nodules. However, recent studies have found that they can occur in up to 18 % of malignant nodules bearing an increased risk of malignancy if there is an interruption in the peripheral calcified edge (probable malignant invasion into the surrounding tissue) (3,5). The analysis of our results did not confirm the prognostic significance of peripheral calcification for the risk of malignancy of thyroid nodules.

**Conclusion:** The presence of microcalcifications and macrocalcifications indicate an increased risk of malignancy and should be taken into account in an integrated assessment of the risk profile of thyroid nodules. Peripheral calcifications are not significant factor for the prognosis of the risk of malignancy of thyroid nodular formations

**References:**

1. Ahn S, E. Kim, D. Kang, S. Lim, J. Kwak, M. Kim, 2010. Biopsy of thyroid nodules: comparison of three sets of guidelines, *AJR Am J Roentgenol.* 194, 31–7.
2. Frates M, C. Benson, J. Charboneau, et al, 2005. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement, *Radiology*, 237, 794–800.
3. Kim B, M. Kim, E. Kim, et al, 2008. Sonographic differentiation of thyroid nodules with eggshell calcifications, *J Ultrasound Med.*, 27, 1425–30.
4. Solbiati L, V. Osti, L. Cova, M. Tonolini, 2001. Ultrasound of thyroid, parathyroid glands and neck lymph nodes, *Eur Radiol*, 11, 2411–24.
5. Yoon D, J. Lee, S. Chang, et al, 200., Peripheral calcification in thyroid nodules, *J Ultrasound Med*, 26, 1349–55.