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**Original Article**

# The Effectiveness of Computed Tomography Texture Analysis in Distinguishing Wilms Tumor from Neuroblastoma

## *Bilgisayarlı Tomografi Doku Analizinin Wilms Tümörünü Nöroblastomdan Ayırt Etmedeki Katkısı*

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## ABSTRACT

**Objective:** This study aimed to determine the effectiveness of computed tomography (CT) texture analysis parameters in distinguishing Wilms tumor (WT) from neuroblastoma (NB).

**Method:** The research included forty-three patients (23 with WT and 20 with NB) with confirmed diagnoses and CT images. Texture analysis involved seven first-order and nine second-order parameters, with receiver operating characteristic (ROC) analysis performed to differentiate between WT and NB.

**Results:** Results showed that the median tumor volume was significantly higher in the WT group. Significant differences were found in entropy and homogeneity among first-order parameters. ROC analysis revealed sensitivity and specificity values: 78% and 45% for uniformity, 56% and 85% for entropy and 47% and 75% for sum entropy.

**Conclusion:** Findings suggest that texture analysis has potential in distinguishing WT from NB in pediatric CT scans, which may reduce the need for repeated scans, additional imaging and invasive procedures, thereby improving patient care and reducing healthcare costs

**Keywords:** Computed tomography, texture analysis, Wilms tumor, neuroblastoma

## ÖZ

**Amaç:** Bu çalışmanın amacı, bilgisayarlı tomografi (BT) doku analizi parametrelerinin Wilms tümörünü (WT) nöroblastomdan (NB) ayırt etmedeki etkinliğini belirlemektir.

**Yöntem:** Araştırmaya doğrulanmış tanıları ve BT görüntüleri olan 43 hasta (23 WT ve 20 NB) dahil edildi. Doku analizi, WT ve NB arasında ayrım yapmak için gerçekleştirilen alıcı işletim karakteristiği analizi ile yedi birinci dereceden ve dokuz ikinci dereceden parametre içeriyordu.

**Bulgular:** Sonuçlar, medyan tümör hacminin WT grubunda anlamlı olarak daha yüksek olduğunu gösterdi. Birinci dereceden parametreler arasında entropi ve homojenlik açısından anlamlı farklılıklar bulunmuştur. ROC analizi, duyarlılık ve özgüllük değerlerini ortaya çıkardı: tekdüzelik için %78 ve %45, entropi için %56 ve %85 ve toplam entropi için %47 ve %75.

**Sonuç:** Bulgular, doku analizinin pediatrik BT taramalarında WT'yi NB'den ayırt etmede potansiyele sahip olduğunu, bunun da tekrarlanan taramalara, ek görüntülemeye ve invaziv prosedürlere olan ihtiyacı azaltabileceğini, böylece hasta bakımını iyileştirebileceğini ve sağlık hizmeti maliyetlerini azaltabileceğini göstermektedir.

**Anahtar kelimeler:** Bilgisayarlı tomografi, doku analizi, Wilms tümörü, nöroblastom

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## INTRODUCTION

Wilms tumor (WT) and neuroblastoma (NB) are the most common intra-abdominal malignant tumors found in adjacent organs in the pediatric age group[(1)]. Because these tumors are frequent in children and typically present with a large abdominal mass, they are often considered in the differential diagnosis of each other, based on clinical and radiological evidence. Diagnostic imaging and laboratory findings are usually helpful in making a definitive diagnosis, but accurately distinguishing between these two tumors can sometimes be challenging[(2)].

Imaging methods are used to gather specific information about tumors, evaluate the type of malignancy, determine the spread of the disease, assess the response to treatment and identify the possible risk of cancer recurrence. However, it is not always possible to distinguish between different types of tumors using

radiological methods. Therefore, a definitive diagnosis of WT or NB before treatment is crucial, as the management and treatment of these tumors are quite different[3]. Nephrectomy is the primary treatment for WT, while neoadjuvant chemotherapy is the main approach for preserving the kidney and its functions in patients with high-risk abdominal NB. WTs typically appear as pseudoencapsulated spherical intrarenal tumors and involve calcification in about 9% of cases, whereas NBs involve calcification in approximately 90% of patients.

Additionally, NB may exhibit radiological findings similar to WT, such as thrombosis in the renal vein, inferior vena cava and right atrium or, in rare cases, lung metastasis. When a large NB infiltrates the kidney, it can be misdiagnosed as an exophytic WT[4].

Computed Tomography Texture Analysis (CTTA) is a new technique that analyses tissue in terms of its structure, microarchitecture, symmetry and homogeneity or heterogeneity[5]. Texture analysis is a quantitative, mathematical image processing method used to assess the spatial heterogeneity of regions of interest in medical imaging and the spatial interrelationships of non-invasive pixel densities. It is used to distinguish between benign and malignant or biologically more aggressive lesions, evaluate tissue microenvironment heterogeneity, tumor grade, tumoral cellular processes, such as hypoxia or angiogenesis, and genetic characteristics such as mutation status, response to treatment and measure fibrosis. In recent years, CTTA has been used in the differential diagnosis of malignant, benign lymphadenopathies in children, in the evaluation of metastatic and non-metastatic lung solid nodules and the diagnosis and grading of immature teratomas[6-8].

This study aimed to retrospectively investigate whether CTTA parameters can distinguish between WT and NB, which are common intra-abdominal tumors in the pediatric age group.

## MATERIALS and METHODS

### Study Design and Patient Selection

This retrospective study, meticulously conducted at a single-center university hospital and approved by the Selçuk University Local Ethics Committee (approval number: 2021/174, date: 07.07.2021), as well as in observance of the ethical principles outlined in the Declaration of Helsinki, aimed to identify sixty patients with pathological diagnoses of WT and NB. After a thorough process of exclusion and careful selection, a total of forty-three patients (23 WT, 20 NB) with pathological diagnoses and computed tomography (CT) images in the Picture Archiving and Communication System were included in the study.

### CT Examination Protocol and Imaging Analysis

The images were obtained using a spiral CT scanner equipped with 64 detectors (Aera, Siemens, Erlangen, Germany) and utilizing low kVp. Axial CT images of the abdomen with a 3.0 mm section thickness were acquired during the venous phase. The specific acquisition parameters were as follows: tube voltage ranging from 110 to 80 kV, tube current from 110 to 180 mA, pitch factor of 0.8, FOV 350-400 mm coverage, single collimation width of 1.2 mm and the use of automatic dose reduction software (CARE Dose 4D). Additionally, a 2 mg/mL non-ionic contrast agent was administered using an auto-injector at a 2-3 mL/sec rate.

### CT Texture Analysis

The CTTA was conducted using OLEA research software (Toshiba Medical Systems, Tokyo, Japan) by a researcher with four years of experience in general radiology and another researcher with ten years of experience in pediatric radiology. The process involved placing a free-hand region of interest (ROI) with a radius of approximately one cm in tumor areas without significant necrosis, calcification or vascular structures, in venous phase sequences (Figures 1, 2). Texture analysis included seven first-order statistical parameters (entropy, mean, median, skewness, kurtosis, variance, uniformity) and nine second-order parameters gray matter co-occurrence matrix (GLCOM) (contrast, informal measure of correlation 2, inverse difference moment, maximum probability, sum average, sum entropy, short-run low gray level emphasis and long-run high gray level emphasis), using grey level run length matrix (GLRLM).

### Statistical Analysis

All the data was processed in Microsoft Office Excel and then transferred to the SPSS (version 21.0, IBM Corp.) for statistical analysis. The Kolmogorov-Smirnov test assessed the data distribution, which examined skewness and kurtosis. The descriptive statistics of the data included minimum, maximum, mean, standard deviation and median, with interquartile range (IQR). Differences between the mean values of patients' age and tumor volume among the tumor groups, were compared using the Mann-Whitney U test. Additionally, differences between the median values of the first order, GLCOM and

GLRLM parameters among WT and NB were compared using the Mann-Whitney U test. Receiver operating characteristic (ROC) analysis was also conducted to differentiate between WT and NB using the first order, GLCOM and GLRLM parameters. Diagnostic results such as sensitivity, specificity, predictive values and diagnostic accuracy were provided at the 95% confidence interval. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

The age range of patients with WT was from 0.1 to 6 years, with a median age of 3 years (IQR: 2-4) and a mean age of 3.17 years with a standard deviation of 1.74. Patients

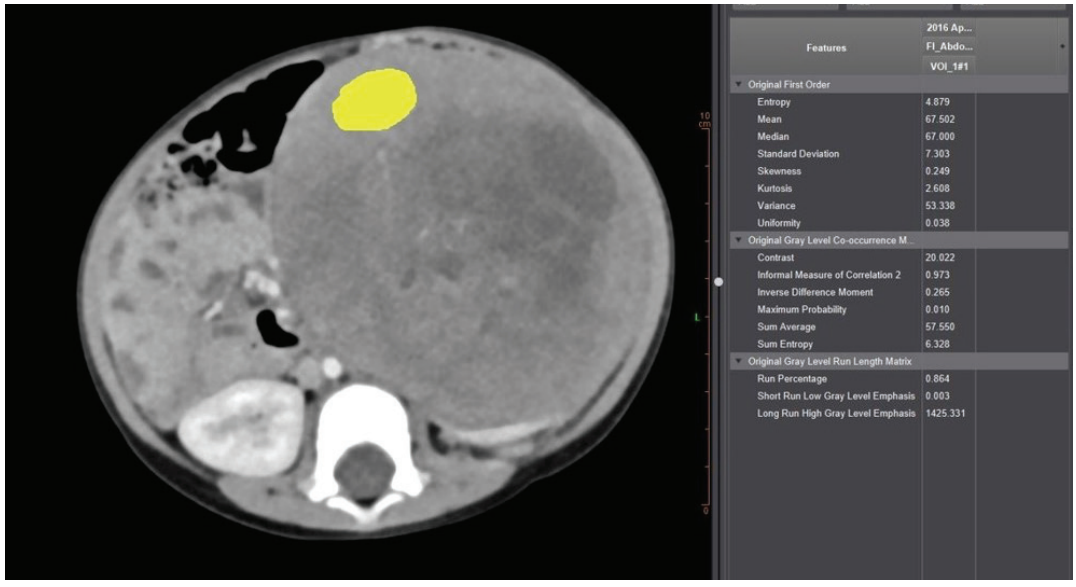


**Figure 1.** Axial contrast-enhanced CT images: the tissue analysis program monitors the ROI area (yellow area) drawn on the solid mass originating from the left kidney, along with the tissue analysis results of the statistical parameters in the case with WT

CT: Computed tomography, ROI: Region of interest, WT: Wilms tumor

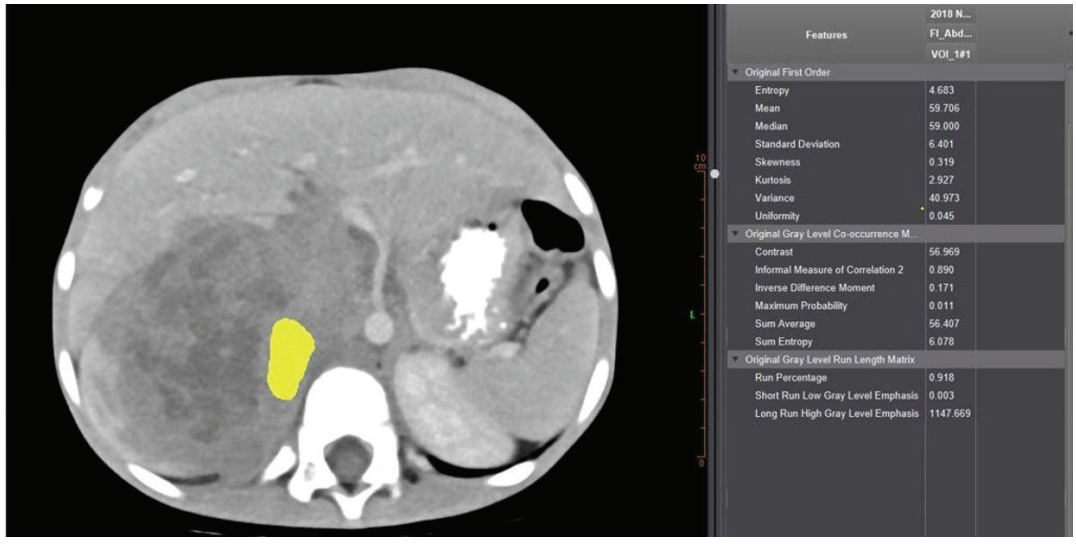


**Figure 2.** Axial contrast-enhanced CT images: in the case of NB, the tissue analysis program monitors the results of the tissue analysis of the ROI area (yellow area) and statistical parameters drawn on the solid mass in the right adrenal area

CT: Computed tomography, ROI: Region of interest, NB: Neuroblastoma

with NB also had an age range from 0.1 to 6 years, with a median age of 1 year (IQR: 1-3) and a mean age of 2 years with a standard deviation of 1.91. The p-value for age comparison between the two groups was 0.023. In terms of tumor volume, patients with WT had volumes ranging from 32 to 2320 mL, with a median volume of 301 mL (IQR: 106-576) and a mean volume of 429 mL, with a standard deviation of 496. In contrast, patients with NB had tumor volumes ranging from 9 to 1012 mL, with a median volume of 105 mL (IQR: 23-278) and a mean volume of 202 mL with a standard deviation of 255. The p-value for tumor volume comparison was 0.013.

Table 1 displays the median values with IQR of the first-order, GLCOM and GLRM parameters. Among these parameters, entropy and uniformity from the first-order parameters and sum entropy from the GLCOM parameters showed statistically significant differences among the tumor groups. Specifically, entropy (p=0.015) and sum entropy (p=0.038) were significantly higher in the NB group compared to the WT group. At the same time, uniformity (p=0.027) was considerably higher in the WT group compared to the NB group.

Moreover, Table 2 presents the ROC analysis results, including the ROC curve for entropy, uniformity and sum entropy to distinguish WT from NB (Figure 3). Sensitivity, specificity, predictive values, diagnostic accuracies and areas under the curves were calculated for the 95% confidence interval cut-off values.

**Table 1. Median and IQR s of the first order, GLCOM and GLRLM parameters compared among WT and NB**

| | Wilms median (IQR) | Neuroblastoma median (IQR) | p-value |
|---|---|---|---|
| Entropy | 4.49 (4.27-4.85) | 4.78 (4.58-5.14) | 0.015 |
| Mean | 58.93 (50.73-71.83) | 61.83 (55.26-82.99) | 0.16 |
| Median | 59 (51-71) | 62.5 (55.2-83) | 0.18 |
| SD | 5.99 (4.75-7.6) | 6.49 (5.87-8.67) | 0.1 |
| Skewness | 0.01 (-0.23-0.5) | 0.007 (-0.22-0.25) | 0.89 |
| Kurtosis | 3.08 (2.76-3.78) | 2.92 (2.61-3.21) | 0.13 |
| Variance | 35.97 (22.57-57.85) | 42.15 (34.51-75.59) | 0.08 |
| Uniformity | 0.05 (0.042-0.059) | 0.045 (0.036-0.049) | 0.027 |
| Contrast | 30.91 (23.7-45.73) | 26.72 (21.16-39.65) | 0.28 |
| Informal measures of correlation | 0.94 (0.92-0.95) | 0.95 (0.93-0.97) | 0.22 |
| Inverse difference moment | 0.22 (0.2-0.25) | 0.24 (0.2-0.26) | 0.18 |
| Maximum probability | 0.015 (0.01-0.016) | 0.011 (0.009-0.016) | 0.21 |
| Sum average | 67.25 (54.6-72.2) | 64.4 (62.8-69.75) | 0.77 |
| Sum entropy | 5.94 (5.63-6.05) | 6.06 (5.81-6.25) | 0.038 |
| Run percentage | 0.87 (0.85-0.89) | 0.88 (0.85-0.9) | 0.3 |
| Short-run low gray level emphasis | 0.003 (0.002-0.005) | 0.003 (0.002-0.003) | 0.34 |
| Long-run low gray level emphasis | 1972 (1327-2121) | 1973 (1326-2120) | 0.75 |

p-values are obtained with the Mann-Whitney U test

SD: Standard deviation, IQR: Interquartile range, WT: Wilms tumor, NB: Neuroblastoma, GLCOM: Gray matter co-occurrence matrix, GLRLM: Grey level run length matrix

**Table 2. ROC curve analysis results of the significant parameters distinguishing Wilms tum WT roblastoma**

| | AUC | Cut-off | Sens % (95% CI) | Spes % (95% CI) | PPV % (95% CI) | NPV % (95% CI) | Diagnostic accuracy % (95% CI) |
|---|---|---|---|---|---|---|---|
| Uniformity | 0.7 | 0.042 | 78 (56-92) | 45 (23-68) | 62 (51-71) | 64 (41-81) | 63 (46-77) |
| Entropy | 0.72 | 4.55 | 56 (34-76) | 85 (62-96) | 81 (58-92) | 63 (50-73) | 70 (54-82) |
| Sum entropy | 0.68 | 5.84 | 47 (26-69) | 75 (50-91) | 68 (48-84) | 55 (43-66) | 60 (44-75) |

WT: Wilms tumor, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval

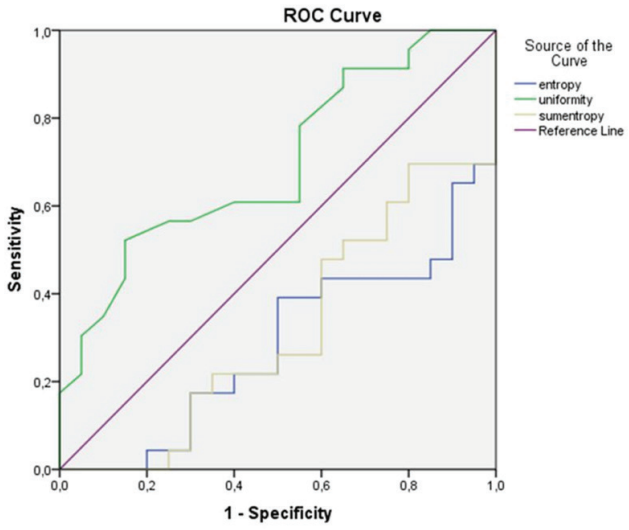


**Figure 3.** ROC curve of the entropy, uniformity and sum entropy used for distinguishing WT from NB

ROC: Receiver operating characteristic, WT: Wilms tumor, NB: Neuroblastoma

## DISCUSSION

NB is the most common solid tumor outside the brain in children, making up 6 to 10% of all pediatric malignancies. It originates from neural crest cells in the adrenal medulla and sympathetic ganglia. Following NB, WT is the second most common pediatric extracranial malignancy, constituting 5 to 6% of pediatric malignancies. The WT is an embryonal renal tumor containing blastemal, stromal and epithelial components. Around 90% of NB s originate in the adrenal gland. Due to their prevalence in the pediatric age group and the typical presentation of a large abdominal mass, these tumors are considered differential diagnoses of each other, from clinical and radiological perspectives.

Differential diagnoses of WT and NB can often be determined through radiological imaging examinations. Features favouring NB include calcification, unclear borders, patient age under two years, crossing the midline, as well as bone and lymph node involvement. Conversely, features of WT include patients aged 3 to 4 years, regular border features, vascular invasion, paw finding and lung metastases. However, radiological differentiation may not always be possible and a definitive diagnosis usually requires a histopathological examination.

While histopathological examination is considered the gold standard for tumor diagnosis, typing and grading in oncological diseases, the medical field is making significant efforts to develop non-invasive methods for prognosis determination, which would reduce the need for treatment and preoperative biopsy[9]. Tissue analysis is a non-invasive, mathematical method that evaluates the spatial heterogeneity of regions of interest in medical imaging[10]. Tissue analysis techniques, first used in radiology by Sutton and Hall[11] in 1972, have become increasingly popular in today's medicine, particularly in the diagnosis, classification and treatment follow-up of oncological diseases. Descriptive statistics revealed that NB was more common in the first two years of age and WT was more common in the 3 to 4 years age group, in line with existing literature. While the size at the time of diagnosis was not previously significant for differentiation in both tumors, this study's results revealed a considerable p-value, indicating that Wilms's tumor was more critical at the time of diagnosis[12].

In this research, we explored the effectiveness of CTTA in distinguishing between WT and NB. Texture analysis assesses the diversity of the cancer and evaluates it based on the disparities in brightness between the examined region and the background signal intensity. Regarding the significant texture parameters in our study, uniformity measures the consistency of gray-level densities within an image or region ROI. Maximum uniformity is achieved when all pixels in an image or ROI, have the same gray level density. Entropy, a measure of heterogeneity, reflects the randomness of the density distribution in the analyzed image. Entropy is at its peak when all densities in the matrix have equal probability. Sum entropy, another indicator of heterogeneity, is calculated by summing the differences between the density values of neighbouring pixels. No prior studies in the literature compare WT and NB regarding texture parameters. In 2009, Shin et al.[13] utilized texture analysis in the differential diagnosis of WT, rhabdoid tumor and clear cell renal sarcomas through ultrasonography, yielding significant results in various texture parameters, such as sum mean, maximum probability and inverse difference moment. Cahalane et al.[6] stated that the use of CTTA features in the study conducted by Pediatric CT, increases the usefulness of pediatric CT in differentiating the difference between benign lymphadenopathy and malignant lymphadenopathy, that it should be added to CT protocols, that it has great potential to aid in the characterization of ambiguous lymph nodes and that it will reduce associated radiation exposure, as well as the need for tissue sampling with follow-up imaging. Our

study is the first to describe the CT texture parameters for both WT and NB.

WT more commonly contains cystic-necrotic areas and bleeding, while calcification is more common in NB. Both tumors appear heterogeneous in radiological and pathological terms. This study aimed to evaluate the microscopic heterogeneity by measuring the tumors' cystic, hemorrhagic and calcific regions. The study found that the uniformity was higher in WT, while the entropy and total entropy were higher in NB, indicating that NB is more heterogeneous at the microscopic level. The study also suggested that specific parameters of the Bi-dimensional Texture Analysis may have good diagnostic performance (area under the curve >0.7) in differentiating NB from WT.

### Study Limitations

Our study has some limitations. Firstly, it was conducted with limited WT and NB cases due to its retrospective and single-center nature. Secondly, since the masses are heterogeneous, ROI measurements were made from the solid part, which may affect the tissue analysis parameters. Third, given the reproducibility of the results, this study only analyzed seven first-order and nine second-order parameters, which did not cover all known tissue features. Since this study is a preliminary attempt to use CTTA to identify and rank the 16 parameters of IT, further research will delve deeper into this area with the support of artificial intelligence and additional parameters. Finally, given the relatively limited research on tissue analysis of CT, the contribution of all tissue features to clinical interpretation has yet to be fully recognized. Future research is required to accumulate additional experience in this field, in order to further validate and elucidate the relevance and mechanisms of textural features in clinical practice.

## CONCLUSION

The research presented in this study illustrates the potential of utilizing textural analysis to differentiate between WT and NB when examining CT scans of pediatric patients. If successfully implemented in standard clinical practice, this method can minimize the requirement for repetitive follow-up scans, additional imaging and invasive tissue sampling procedures. By incorporating tissue analysis into the existing pediatric abdominal CT protocols, medical professionals may be better equipped to accurately diagnose and differentiate between WT and NB using imaging alone. However, further comprehensive studies with larger sample sizes remain essential to validate the practicality of distinguishing between WT and NB, within real-world clinical environments.

### Ethics

**Ethics Committee Approval:** The study was approved by the Selçuk University Local Ethics Committee (approval number: 2021/174, date: 07.07.2021).

**Informed Consent:** Retrospective study.

### Author Contributions

Concept: A.G., B.K., Z.İ.B., M.Ö., Design: A.G., İ.A., B.K., Z.İ.B., M.Ö., Data Collection and Processing: A.G., İ.A., B.K., M.Ö., Y.K., Analysis and Interpretation: İ.A., Z.İ.B., M.Ö., Y.K., Literature Search: M.Ö., Y.K., Writing: M.Ö.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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