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Research article

Assessment of Thyroid Gland in Children with Point-of-Care Ultrasound (POCUS): Radiological Performance and Feasibility of Handheld Ultrasound in Clinical Practice

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What is already known about this topic?
Point-of-Care Ultrasound (POCUS) refers to the use of portable ultrasound machines to perform quick and focused ultrasound examinations at a patient's bedside or point-of-care. POCUS can be performed by all health workers with specific training to use POCUS.

What this study adds to the literature?
This study aimed to investigate the radiological performance and feasibility of POCUS using a handheld ultrasound (HHUSD) system in children from the perspective of the thyroid gland.
A pediatric endocrinologist, equipped with sufficient training in thyroid US evaluation, incorporates the HHUSD as a routine tool for clinical examinations in outpatient settings, they can effectively assess normal thyroid tissue in pediatric patients. Moreover, the HHUSD system proves to be useful in detecting thyroid pathologies.

Abstract
Background: Point-of-Care Ultrasound (POCUS) refers to the use of portable ultrasound machines to perform quick and focused ultrasound examinations at a patient's bedside or point-of-care. POCUS can be performed by all health workers with specific training to use POCUS. This study aimed to investigate the radiological performance and feasibility of POCUS using a handheld ultrasound (HHUSD) system in children from the perspective of the thyroid gland perspective.
Material-Methods: A pediatric endocrinologist performed thyroid imaging in children referred to our hospital with suspected thyroid disease using an HHUSD system. The same children underwent US imaging using the same device by the first radiologist, and a second radiologist performed thyroid US using an advanced high-range Ultrasound Device (AHUSD) (defined as the gold-standard method) within two hours. The data obtained by the three researchers were compared with each other.
Results: This study included 105 patients (68.6% girls [n=72)]; mean age 12.8±3.6 years]. When the thyroid volume was evaluated, a strong correlation was found between the measurements of the three researchers (AA vs. MG: r=0.963, AA vs. GT: r=0.969, MG vs. GT: r=0.963, p<0.001). According to the Bland-Altman analysis, for total thyroid volume, AA measured 0.43 cc (%95 CI: -0.89-0.03) smaller than MG, and 0.11 cc (%95 CI: -0.30-0.52) larger than GT, whereas MG measured 0.52 cc (%95 CI: 0.09-0.94) larger than GT. When evaluated for the presence of goiter and nodules, a near-perfect agreement was found between the results of the three researchers (AA vs GT; κ=0.863, MG vs GT; κ=0.887, p<0.001, and AA vs GT; κ=1.000, MG vs GT; κ=0.972, p<0.001, respectively). When evaluated in terms of the longest axis of nodules, a high correlation was found between the measurements of the three researchers (AA vs MG; r=0.993, AA vs GT; r=0.996, MG vs GT; r=0.996, p<0.001). When evaluated in terms of the final diagnosis, the evaluations of the three researchers showed excellent agreement with each other (AA vs GT; κ=0.893, MG vs GT; κ=0.863, p<0.001, Accuracy rate AA vs GT: 93.3%; MG vs GT: 91.4%).
Conclusion: A pediatric endocrinologist, equipped with sufficient training in thyroid US evaluation, incorporates the HHUSD as a routine tool for clinical examinations in outpatient settings, they can effectively assess normal thyroid tissue in pediatric patients. Moreover, the HHUSD system proves to be useful in detecting thyroid pathologies. However, it is crucial to note that for a more comprehensive evaluation of thyroid nodules, including detailed assessment and Thyroid Imaging Reporting and Data System "TIRADS" classification, patients should be referred to radiology departments equipped with AHUSD systems. These specialized devices, along with the expertise of radiologists, are essential for in-depth evaluations and accurate classification of thyroid nodules.
Keywords: Handheld ultrasound, imaging, pediatric, point-of-care ultrasound, tyroid pathologies

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Introduction

Sonographic evaluation of the thyroid gland is routinely performed by radiologists to diagnose various thyroid diseases in children, including autoimmune thyroiditis, thyroid nodules, thyroid cancer, and goiter [1,2]. Effective communication between clinicians and radiologists is crucial for accurate assessment and proper management of these conditions [3].
With advancements in ultrasonography (US) technology, the range of US products has expanded to include mobile devices that enable bedside examinations. These devices complement the traditional fixed US equipment found only in radiology departments. Commonly referred to as Point-of-care ultrasound (POCUS) in literature, these devices are categorized into three types: laptop-associated devices, hand-carried systems, and handheld ultrasound systems (HHUSD). The introduction of these systems brings us closer to the realization of the ultrasound stethoscope concept [4].
The advancements in POCUS technology are outpacing the clinical studies conducted on the clinical performance of these technologies. Therefore, we believe that further research should be conducted to assess the clinical performance of these technologies. Such studies are crucial for advancing the development of this technology and realizing the concept of the ultrasound stethoscope. We propose that these studies should encompass various organ systems, different pathologies, and even different age groups. Clinical performance is influenced by both the device's capabilities and the proficiency of the user.

Handheld ultrasound systems have gained significant interest and attention in recent years [5]. Studies have shown that they have high diagnostic accuracy and can be used for various applications such as abdominal, cardiac, and musculoskeletal imaging [6,7]. However, there is no research specifically on the use of HHUSD for thyroid imaging in children. In this study, we focused on evaluating the clinical performance of HHUSD in children with suspected thyroid disease. We conducted a comparison between the HHUSD system and the gold standard Advanced high-range Ultrasound Device (AHUSD) and aimed to assess the performance of pediatric endocrinologists who have received sufficient basic training in thyroid US. We evaluated the performance of a pediatric endocrinologist and two radiologists who had substantial expertise in conducting thyroid US. By considering both user expertise and device performance, we aimed to gain comprehensive insights into the clinical application of HHUSD systems for thyroid imaging in children.

Material and Methods

Study Subjects

The university hospital where the study was conducted is a tertiary healthcare center located in a city with a population of over 1,000,000. It is the only pediatric endocrinology center in the city and provides services to all types of pediatric endocrinology patients. This study included pediatric patients aged 5-18 years who were referred to our hospital with suspected thyroid disease (neck swelling, hypothyroidism or hyperthyroidism symptoms, family history of thyroid diseases, abnormalities in thyroid function tests, etc.).

Height was measured using a Harpenden stadiometer with a precision of 0.1 cm, while weight was measured using a scale with a precision of 0.1 kg (SECA, Hamburg, Germany). Subjects were weighed with all clothing removed, except for undergarments. Body Mass Index (BMI) was calculated by dividing weight (kg) by the square of height (m^2). A BMI at or above the 95th percentile, according to data from healthy Turkish children defined as obesity [8]. Serum thyroid hormones, anti-thyroid peroxidase (TPO), and anti-thyroglobulin (TG) levels were measured using standard methods on blood samples obtained from all patients under appropriate conditions.

Ultrasonography

After obtaining informed consent from the patients and their parents, a pediatric endocrinologist (AA) with 13 years of clinical experience in pediatric endocrinology and 1 year of thyroid US experience performed thyroid US imaging at the out-patient clinic using a Sonostar C5PL HHUSD (Sonostar Technologies Co Ltd, Guangzhou, China). Within 2 hours, the same patients underwent thyroid US imaging using the same device (Sonostar C5PL HHUSD) by a radiologist (MG) with 15 years of experience and lastly, a detailed thyroid US imaging, using AHUSD Samsung RS80 (Gyeonggi-do, Republic of Korea) with LA2-9A linear probe by another experienced radiologist (GT) with 16 years of experience, was performed to the same patients. The US data obtained by the pediatric endocrinologist and two radiologists were noted in detail. The 3 dimensions of the thyroid gland (anterior-posterior "AP", medio-lateral "ML" and longitudinal "Long"), volume, parenchymal echogenicity, size of any nodules, composition (solid, semisolid, cystic), and echogenicity of the dominant nodule, and final sonographic diagnosis were recorded. The calculation of the volume for each lobe was done individually using the formula for an ovoid (Depth x Length x Width x pi/6) [9]. The total thyroid volume was then determined by adding the volume of both lobes together. Thyroid volume SDS was calculated using the normal range for Turkish children [10]. Those with a total thyroid volume >2 SDS were considered to have a goiter. To isolate the operator from device performance, we separately compared the pediatric endocrinologist who used HHUSD to the radiologist using the same device (AA vs. MG) and we also compared the radiologist who used HHUSD to the radiologist who used AHUSD (MG vs. GT). Lastly, we compared the pediatric endocrinologist who used HHUSD to the radiologist who used AHUSD (AA vs. GT).

Final Diagnosis [11]

Normal: Patients with euthyroidism, negative anti-TPO and anti-TG, and normal US findings.

Hashimoto's thyroiditis: Patients with euthyroidism/hypothyroidism, positive anti-TPO and anti-TG, and ultrasound findings consistent with thyroiditis.

Graves' disease: Patients with hyperthyroidism, positive anti-TPO and anti-TG, and ultrasound findings consistent with thyroiditis.

Obesity-related changes: Patients with euthyroidism, negative anti-TPO and anti-TG, and parenchymal heterogeneity on ultrasound.

Statistical Analysis

The statistical analysis for this study was performed using IBM SPSS Statistics version 27.0 (IBM Corp, Released 2020, Armonk, NY: IBM Corp) and NCSS 11 (NCSS 11 Statistical Software, 2016, NCSS, LLC, Kaysville, Utah, USA, ncss.com/software/ncss). The normality of the data distribution was assessed through descriptive statistics, kurtosis and skewness coefficients, histograms, and the Shapiro-Wilk test. As the data were found to be non-normally distributed, Friedman's test was used to compare the three groups. Pearson and Spearman's correlation tests were employed for correlation analyses. Kappa and intraclass correlation coefficient (ICC) statistics were utilized to assess agreement. The agreement between the US measurements was evaluated using the Bland-Altman method. Type 1 error was determined as 5%.

Results

A total of 105 children [68.6% (n=72) girl] were included in the study. The mean age was 12.8±3.6 years [13.0 (4.7-18.0)]. The reasons for referral to our hospital were as follows: 72.4% (n=76) for abnormal thyroid function tests, 17.1% (n=18) for neck swelling, 5.7% (n=6) for symptoms of hyperthyroidism, and 4.8% (n=5) for symptoms of hypothyroidism. The clinical and laboratory characteristics of the subjects were given in Table 1.

There was a strong positive correlation between AA vs. MG, AA vs. GT, and MG vs. GT in terms of total thyroid volumes (r=0.963, 0.969, 0.963, p<0.001, respectively) (Table 2). The ICC for thyroid volumes was 0.963 (95% confidence interval: 0.949-0.974). In the Bland-Altman analysis performed in terms of the correlation of detailed US measurements (right thyroid volume, left thyroid volume and total thyroid volume) a strong correlation was found between the measurements. The difference between the measurements in terms of total thyroid volume was -0.43 (95% CI [-0.89]-0.03) for AA vs. MG; 0.11 (95% CI [-0.30]-0.52) for AA vs. GT; 0.52 (95% CI 0.09-0.94) for MG vs GT (Table 2, Figure 1).

When evaluated in terms of the presence of goiter, the measurements of all three researchers showed near-perfect agreement (AA vs. MG; κ=0.887, AA vs. GT; κ=0.863, MG vs. GT; κ=0.889, p<0.001). The measurements of all three researchers demonstrated substantial agreement when assessing parenchymal echogenicity. (AA vs. MG; κ=0.685, AA vs. GT; κ=0.771, MG vs. GT; κ=0.730, p<0.001). A near-perfect agreement was observed among all three researchers' evaluations when assessing the presence of nodules (AA vs. MG; κ=0.972, AA vs. GT; κ=1.000, MG vs. GT; κ=0.972, p<0.001) (Table 3).

When evaluated for the presence of nodules and considering AHUSD as the gold standard method, nodules were detected in a total of 23 patients (22%). Among these cases, 43.5% (n=10) were identified as cystic nodules, 21.7% (n=5) exhibited semisolid nodules, and 34.8% (n=8) presented with solitary nodules (AA vs. MG; κ=0.864, AA vs. GT; κ=0.864, MG vs. GT; κ=0.858, p<0.001). The features that can predict malignancy in solid nodules, such as irregular margins and microcalcifications could not be evaluated with HHUSD. When evaluated in terms of the last diagnosis according to the AHUSD 23.5% (n=25) of the patients were diagnosed as normal, 40.0% (n=42) had Hashimoto's thyroiditis, 16.2% (n=17) had coexistence of nodules and thyroiditis, 7.5% (n=8) had Graves' disease, 6.7% (n=7) had obesity-related changes, and 5.6% (n=6) had solitary nodules (Table 1). The final diagnoses of all three researchers showed near-perfect agreement (AA vs. MG; κ=0.871, AA vs. GT; κ=0.910, MG vs. GT; κ=0.884, p<0.001). The ICC for the long axis of the nodule was 0.995 (0.989-0.998). In the Bland-Altman analysis performed in terms of the correlation of nodule size, a strong correlation was found between the measurements. The difference between the measurements of the nodule size was 0.49 (95% CI [-0.30]-1.27) for AA vs. MG; 0.26 (95% CI [-0.32]-0.83) for AA vs. GT; -0.25 (95% CI [-0.87]-0.38) for MG vs GT (Figure 2).

Discussion

The results of the present study showed a high correlation and perfect agreement between the measurements and evaluations of the three researchers in terms of three-dimensional measurements of the thyroid, thyroid volume, presence of goiter, presence of nodules, the longitudinal plane of nodules, and final diagnosis. Additionally, the Bland-Altman analysis showed that the differences in measurements between the researchers were within acceptable limits. This study is the first clinical trial demonstrating the effectiveness of HHUSD performed by clinicians in the thyroid US examination in children.

Thyroid US is a gold standard imaging modality in the evaluation of thyroid nodules and other thyroid disorders [12,13]. However, the accuracy of this imaging modality depends on several factors including the experience and skill of the user, the ability to integrate US findings with the patient's clinical history and examination, and the quality of the US device. The US is a highly accurate modality when performed by an experienced user [14]. However, clinical findings are an important part of the accurate final diagnosis, so these findings need to be shared between the clinician and the radiologist. Several studies have shown that integrating clinical information with US findings can improve the diagnostic accuracy of thyroid US [15,16]. Due to the significant outpatient workload in radiology departments, obtaining a US examination can pose challenges. If HHUSD were part of the clinical evaluation by the clinician, this would eliminate the unnecessary workload for the radiology departments [17,18].

POCUS systems have become an integral part of patient evaluation in departments such as emergency services, anesthesia, intensive care, and general surgery, where triage or urgent assessment is required. They are now incorporated into the curriculums and guidelines of these specialties [19]. The widespread availability of HHUSD has made accessing POCUS systems easier, leading to increased utilization of these systems [20]. At this point, the question arises as to whether POCUS systems should be included as part of the physical examination during routine outpatient services, not just for patients requiring urgent evaluation. If HHUSD becomes part of the examination, it would enable radiology departments to provide intensive outpatient services to minimize unnecessary patient burden and ensure triage for patients who require this service [21]. Consequently, this could reduce the number of unnecessary diagnostic tests and decrease the unnecessary costs imposed on the healthcare system.

The results of our study indicate that the effective use of POCUS systems relies on two essential components. The first component pertains to the appropriateness of the HHUSD system used for the specific organ system, while the second component relates to the user's adequate knowledge and skill level for conducting sonographic examinations. Our study demonstrates that HHUSD when employed by a properly trained clinician exhibits a strong correlation with the gold standard, which involves the utilization of AHUSD by an expert radiologist specialized in sonography. In this study, the HHUSD method proved to be effective in detecting thyroid nodules and distinguishing between cystic and solid nodules. However, limitations in the device's resolution capabilities hindered its ability to adequately address features indicative of malignancy in solid nodules, such as the presence of microcalcifications and irregular margins. Given the limited number of patients with solid nodules in our study, making definitive conclusions is challenging, emphasizing the necessity for more comprehensive research on the role of these devices in Thyroid Imaging Reporting and Data System (TIRADS) scoring. These findings emphasize the current limitations of HHUSD systems and underscore the necessity for further advancements in their development. Furthermore, specialties seeking to integrate these systems into routine clinical practice must ensure that proper training is incorporated into their educational programs. In this regard, we propose the inclusion of radiology rotations during pediatric endocrinology training for these specialties and the implementation of certification programs that require periodic retraining in this area following the completion of residency.

Our study possesses several notable strengths. Firstly, we utilized two distinct US systems, providing a comparative analysis between them. Secondly, the participation of a clinician along with two radiologists in the study ensured diverse perspectives and expertise in the evaluation process. Additionally, our patient group consisted of both individuals with normal thyroid function and those with various thyroid pathologies, enabling a comprehensive comparison of normal and pathological data. Furthermore, we implemented an internal evaluation process wherein measurements were independently assessed by the observers at different times, ensuring a blind evaluation unaffected by each other's observations. These strengths collectively enhance the robustness and validity of our study.

Our study does have certain limitations that should be acknowledged. Firstly, it is important to note that there are various generations of HHUSD systems available in the market, but we utilized a standard device for our evaluation. Therefore, the findings may not directly generalize to other generations or models of HHUSD systems. Secondly, our study focused on evaluating the performance of the HHUSD system specifically on thyroid tissue, which is a superficial tissue. It is worth mentioning that the performance of US devices may vary when imaging deeper tissues. Thus, our study's results may not fully reflect the performance of HHUSD systems in imaging deep tissues. Considering these limitations, future studies should explore the performance of different generations or models of HHUSD systems on various tissue types, including deeper structures, to provide a more comprehensive understanding of their capabilities and limitations.

In summary, our study demonstrated that when a pediatric endocrinologist, equipped with sufficient training in thyroid US evaluation, incorporates the HHUSD as a routine tool for clinical examinations in outpatient settings, they can effectively assess normal thyroid tissue in pediatric patients. Moreover, the HHUSD system proves to be useful in detecting thyroid pathologies. However, it is crucial to note that for a more comprehensive evaluation of thyroid nodules, including detailed assessment and TIRADS classification, patients should be referred to radiology departments equipped with AHUSD systems. These specialized devices, along with the expertise of radiologists, are essential for in-depth evaluations and accurate classification of thyroid nodules.

Ethics Committee Approval: Institutional Ethics Committee of Aydın Adnan Menderes University was provided (protocol no: 2022/142, date: 25.08.2022).

Informed Consent: Informed consent was obtained from those included in the study.

Conflict of Interest: The authors declare they have no any financial relationships with the company products used in this study.

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Authorship Contributions

Surgical and Medical Practices: A.A, M.G, G.T, Concept: A.A, M.G, Design: A.A, M.G, Data Collection or Processing: A.A, G.T, Analysis or Interpretation: M.G, G.T, Literature Search: M.G, G.T, Writing: A.A, M.G, G.T.

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Table 1. The clinical and laboratory characteristics of the subjects.

	Mean±SD or % (n)
Age (years)	12.8±3.6
Gender (girl)	68.6 (72)
Height - SDS	0.1±1.2
Weight - SDS	0.2±1.5
Body mass index - SDS	0.2±1.4
Complaint	
Abnormalities in thyroid tests*	72.4 (76)
Neck swelling	17.1 (18)
Symptoms of hyperthyroidism	5.7 (6)
Symptoms of hypothyroidism	4.8 (5)
Free T3 (pg/mL)	4.7±4.2
Low	1.6 (1)
Normal	70.5 (43)
High	27.9 (17)
Free T4 (ng/dL)	1.1±0.5
Low	1.9 (2)
Normal	88.6 (93)
High	9.5 (10)
TSH (uIU/mL)	3.1±5.5
Low	13.3 (14)
Normal	72.4 (76)
High	14.3 (15)
Anti TPO (IU/mL)	259.5±391.7
Positive	42.9 (39)
Anti TG (IU/mL)	107.2±239.9
Positive	49.4 (43)
Final Diagnosis	
Normal	23.8 (25)
Hashimoto thyroiditis	40.0 (42)
Nodule + Hashimoto thyroiditis	16.2 (17)
Graves' disease	7.5 (8)
Obesity related changes	6.7 (7)
Solitary nodule	5.6 (6)

*Patients were referred from another hospital due to abnormal thyroid tests (high or low TSH, high fT3 etc) during screening.

Table 2. Comparison of thyroid volumes

		Right Thyroid Volume	Left Thyroid Volume	Total Thyroid Volume
AA vs. MG	Mean of differences	-0.46	0.03	-0.43
	Upper limit of 95% CI	-0.80	-0.18	-0.89
	Lower limit of 95% CI	-0.13	0.25	0.03
	r	**0.934**	**0.968**	**0.963**
	p	**<0.001**	**<0.001**	**<0.001**
AA vs. GT	Mean of differences	0.08	0.03	0.11
	Upper limit of 95% CI	-0.19	-0.19	-0.30
	Lower limit of 95% CI	0.35	0.26	0.52
	r	**0.956**	**0.960**	**0.969**
	p	**<0.001**	**<0.001**	**<0.001**
MG vs. GT	Mean of differences	0.53	-0.02	0.52
	Upper limit of 95% CI	0.23	-0.28	0.09
	Lower limit of 95% CI	0.84	0.24	0.94
	r	**0.938**	**0.955**	**0.963**
	p	**<0.001**	**<0.001**	**<0.001**

Table 3. Comparison of goiter, parenchymal heterogeneity, and nodule.

		Goiter			**Parenchymal Heterogeneity**			**Nodule**		
		Radiologist Handheld US (MG)		**Kappa p**	**Radiologist Handheld US (MG)**		**Kappa p**	**Radiologist Handheld US (MG)**		**Kappa p**
		Positive	**Negative**		**Positive**	**Negative**		**Positive**	**Negative**	
Pediatric Endocrinologist (AA)	**Positive**	71	4	0.887 <0.001	66	8	0.685 <0.001	82	0	0.972 <0.001
	Negative	1	29		6	25		1	22	
		Radiologist Standard US (GT)			**Radiologist Standard US (GT)**			**Radiologist Standard US (GT)**		
Pediatric Endocrinologist (AA)	**Positive**	71	4	0.863 <0.001	69	5	0.771 <0.001	82	0	1.000 <0.001
	Negative	2	28		5	26		0	82	
Radiologist Handheld US (MG)	**Positive**	70	2	0.889 <0.001	67	5	0.730 <0.001	82	1	0.972 <0.001
	Negative	3	30		7	26		0	22	

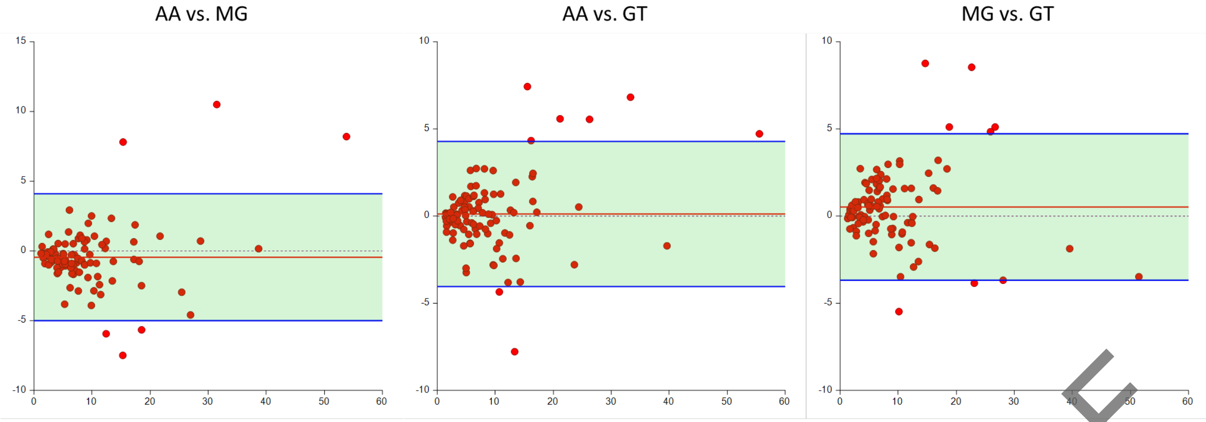

Figure 1. Bland-Altman analysis for total thyroid volumes. Red line (-0.43, 0.11, 0.52) is the bias (average of the differences between total thyroid volumes of AA vs. MG, AA vs. GT, MG vs. GT; respectively). Blue lines ([-5.00]-4.14, [-4.04]-4.26, [-3.67]-4.71) are the limits of agreement, respectively.

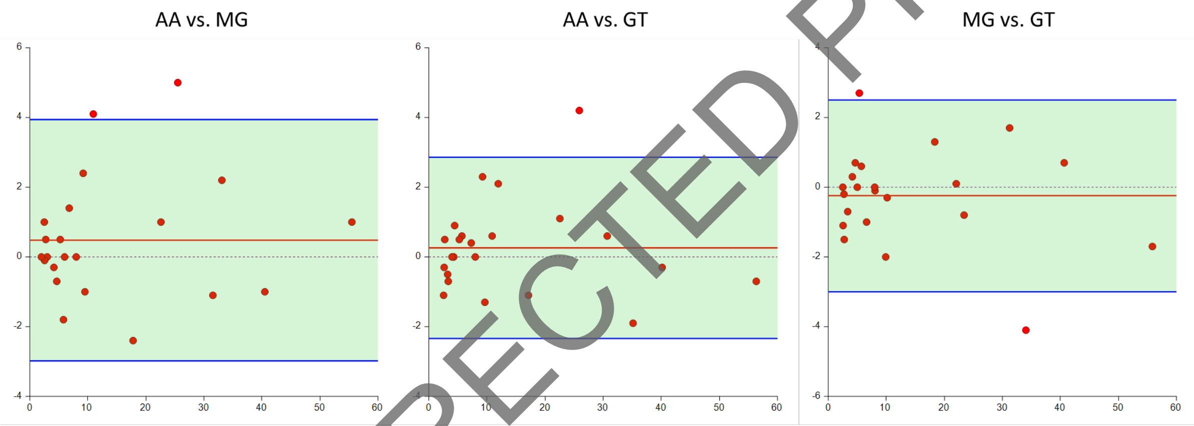

Figure 2. Bland-Altman analysis for nodule long axes. Red line (0.49, 0.26, -0.25) is the bias (average of the differences between nodule long axes of AA vs. MG, AA vs. GT, MG vs. GT; respectively). Blue lines ([-2.96]-3.94, [-2.34]-2.86, [-2.97]-2.53) are the limits of agreement, respectively.