Heliyon 10 (2024) e23777

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Assessment of unilateral condylar hyperplasia with quantitative SPECT/CT

Pingan Liu [a,*], Jun Shi [b]

[a] Department ofNuclear Medicine, China
[b] Department of Oral and Craniomaxillofacial Science, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

A R T I C L E I N F O

Keywords:
Quantitative SPECT/CT
Standardized uptake value(SUV)
99mTc-Methylene diphosphonate(99mTc-MDP)
Unilateral condylar hyperplasia (UCH)

A B S T R A C T

Purpose: The current study aimedto assess condylar activityin patients with unilateral condylar hyperplasia (UCH) with quantitative SPECT/CT.
Patients and methods: This retrospective study included patients with UCH who underwent quantitative SPECT/CT. SPECT analysis and quantification of SPECT/CT were performed, and the maximum count per pixel and SUVmax of either side of the condyles were calculated.
Results: 39 patients were included in the analysisand classified into three subgroups according to the percentile differential right-left ratio: inactive group, left active (LA) group, and right active (RA) group. Totally, the SUVmax of the affected side is significantly higher than the unaffected side (active:5.93 ± 2.43 vs inactive:3.62 ± 1.76, $P < 0.001$), SUVmax-based ratios correlated well with the ratios based on maximum count ($R = 0.944$, $P < 0.001$). ROC analysis showed poorSUVmaxperformance in differentiation between theactive condyles and the inactive condyles due to the lower area under the curve (AUC) (0.588). In subgroup analysis, the affected side is significantly higher than the unaffected side in active groups with SUVmax, no significant difference was found between the active sides or the inactive sides of active groups. Interestingly, the SUVmax of the left side was statistically higher than that of the right sidein the inactive group ($P = 0.01$),while the left side of the right active group has significantlylower activitythan that in the inactive group, meanwhile,the right side showed no significant difference. Furthermore, each side showed no significant difference between the left active group and the inactive group.
Conclusions: SUVmax is not an optimal measurement effectively used to evaluate active condyles. However, SUV ratios correlated well with the count ratios, and the left side of condyles showed a peculiar feature in condyle growth status reflected in radioactivity quantified with SPECT/CT, which needs further study to determine the role in the development of the UCH.

1. Introduction

Unilateral condylar hyperplasia (UCH) of the mandible is a rare pathological condition, which causes facial asymmetry [1,2]. It mainly affects people in adolescence or young adulthood, with a higher prevalence in females than males with more than 64 % of those presenting with the condition being female, according to a systematic review [3].

The etiology of UCH is unclear. Many factors could contribute to unilateral abnormal growth: traumas, heredity or genetics,

* Corresponding author. Department of Shanghai Ninth People's Hospital Medical School of Jiaotong University 639 Zhizaoju Road, Shanghai, 200011, China.

E-mail address: Liupingan9@sina.com (P. Liu).

https://doi.org/10.1016/j.heliyon.2023.e23777
Received 26 April 2023; Received in revised form 29 November 2023; Accepted 13 December 2023
Available online 15 December 2023

hormonal dysfunctions, infections, and arthrosis, but conclusive evidence is lacking [4]. The histological characteristics of the condition constituted an undifferentiated mesenchymal layer, a hyperplastic cartilage layer, and pathognomonic cartilage “islands” in the proximal bony trabeculae [5,6].

Condylar hyperplasia couldbedivided into two functional statuses: active growth andinactive growth [7]. The status of growth of the condyle of hyperplasia enables different strategies of treatments. The active UCH is determined by combining the patient’s history, serial clinical and radiological analysis and bone scintigraphy [8].

Bone scintigraphy has been established as a successful technique to distinguish between active and inactive growth with a pooled sensitivity of 0.71 (95%CI:0.57–0.82) [9]. In recent years, single photon emission computed tomography (SPECT) has been used as a more accurate and reliable method than the initial bone planar scintigraphy for evaluation of condylar uptake with apooled sensitivity valueof 0.90 (95%CI:0.79–0.97) and a pooled specificity value of 0.95 (95%CI:0.82–0.99) [9]. However, recent reports have shown poor specificity (36.1–78.3 %) and sensitivity (32.4–81 %) of SPECT as a diagnostic test [10,11].

Hybrid scanners of SPECT/CT were superior to conventional SPECT and planar scintigraphy, as has been confirmed in various studies [12–14]. Especially, the calculation of Standardized Uptake Values (SUVs) in reconstructed SPECT/CT images from patient studies is feasible within an acceptable error range. SUV is a semiquantitative measure indicating the tracer concentration corrected by body weight and injected activity [15]. SUVs are effective indicators in the assessment of abnormalities [12]. There area few studies of quantitative assessment of UCH with 18F–NaF PET/CT [16–19]. The aim of the study was to explore the utility of quantitative SPECT/CT in assessing UCH with an attempt to find if there is a cut-off value in SUV to evaluate the active status of condyles of UCH patients.

2. Methods

2.1. Patients

Our analysis was approved by the hospital ethics committee (Approval No.:SH9H-2023-T198-2,Shanghai Ninth People’s Hospital, Shanghai Jiaotong University School of Medicine Ethics Committee). Due to the retrospective nature of the analysis, written consents from the patients were waivered. From our clinical database, we retrieved image datasets from patients with unilateral condylar hyperplasia who underwent standard SPECT/CT studies between August 2021 and December 2021.

Patients with conditions of previous trauma or surgery to the temporomandibular joint (TMJ), previous mandibular fractures, neoplastic pathology of TMJ, systemic diseases, or congenital conditions that could potentially affect the TMJ were excluded from the evaluation.

2.2. Quantitative bone SPECT/CT

Patients’ weight, height, syringe dose before and after injection, time of measurement, and injection time were recorded. Patients were administered a radiolabeled agent through the cannula into the superficial vein on the arm, the precise injected dose was calculated by measuring the syringe doses before and after injection. The patients were intravenously injected with 555–851 MBq (15–23 mCi) of 99mTc-MDP for imaging, depending on their body weight (14.8 MBq/kg).

SPECT/CT scanner (NM/CT670; GE Healthcare, USA)was used to acquire quantitative SPECT/CT images. CT images without any contrast wereacquired using a tube voltage of 120 kV with a tube current of auto mA (60–210 mA). An adaptive statistical iterative reconstruction algorithm (ASiR, GE Healthcare) was used to reconstruct CT images into 2.5-mm-thick transaxial slices with a 512 × 512 image matrix. Other CT image acquisition parameters include: X-ray collimation of 20 mm (16 × 1.25 mm),table speed of 37 mm/s,table feed per rotation of 18.75 mm per rotation, tube rotation time of 0.5 s, pitch of 0.938:1. The CT images of 2.5 mm thick sections were reconstructed with adaptive statistical iterative reconstruction algorithm (ASiR; GE Health care). SPECT images were acquiredusing step-and-shoot mode (16 s per step and 60 steps per detector) and a zoom factor of 1.14 with a photon peak of 140 keV (10 % window) and a scatter window of 120 keV (5 % window). SPECT images were reconstructed with an iterative ordered subset expectation maximization algorithm (2 iterations and 10 subsets) with CT-based attenuation correction, scatter correction, and resolution recovery using vendor-supplied software (Volumetrix MI; GE Healthcare). An image matrix of 128 × 128 with a section thickness of 2.95 mm and a zoom factor of 1.5 was reconstructedwithapost-reconstruction filter (Butterworth filter with frequency of 0.48 and order of 10).

2.3. Image analysis

A transaxial frame containing condyles was used to visualize condyles and VOIs were drawn. An identical VOI of 1.8 $cm^3$was applied to either side of the condyles to obtain the maximum count per pixel. The ratio of countsbetween the condyles of the same patientwas calculated for relative uptake. The presence of increased uptake in the condyle of more than 10 % in comparison with the opposite side was considered to be active.

Quantification of SPECT/CT imageswas processed with theQ.Metrix program (GE Healthcare) Volumes of interest (VOIs) were manually drawn on CT images and were projected on the SPECT images, corresponding maximum SUVs (SUVmax)which were corrected by body weightwere recorded. The ratio of SUVmax between the condyles of the same patientwas also calculated.

2.4. Statistical analysis

A Mann-Whitney *U* test (independent samples) or Wilcoxon test (paired samples)was used to test the differences between the variables. A two-sided Spearman's rank correlation coefficientwas used to test correlations. Significance was acceptedwhen $P < 0.05$.

Quantitative measures, including tracer activity concentration expressed in maximum SUV. The description of data is presentedby providing their mean values and their standard deviations (SD).

The receiver operating characteristic curve (ROC) curve and the corresponding area under the curve (AUC) were calculated with active condyles versus inactive condyles for both all the condyles and for each side of condyles in the study. We used the scale of Hosmer and Lemeshow [20], The authors use this scale for interpreting the value of a test in discriminating health from disease: AUC of 0.5–0.7: poor discrimination; 0.7–0.8: acceptable discrimination; 0.8–0.9: excellent discrimination; >0.9: outstanding discrimination.

Statistical analysis was performed using SPSS(version 22,IBM,Armonk, New York, USA).

3. Results

3.1. Characters of patients

Thirty-nine patients (female:23,male:16) with condylar hyperplasia were included in the study, the mean age was 21.31 ± 3.28years (Table 1). The data were classified into three subgroups of the status of condylar activities according to the percentile differentialright-left ratio: the inactive group, the left active (LA) group, and the right active (RA) group. 11 patients (female 6, male 5) were grouped in the inactive group with age of 19.09 ± 1.04 years, 12 patients (female7,male5) in the left active group with age of 22.16 ± 2.65 years,16 patients in the right active group with age of 22.18 ± 3.50 years. The average age of the inactive group was significantly lower than the other active group ($P < 0.01$), and the gender compositions of the three subgroups were not statistically significant ($P > 0.05$).

3.2. Comparison of SUVmax between the activeside and the inactiveside

Totally, the meanSUVmax of the active side of condyles is significantly higher than the inactive side (active:5.93 ± 2.43 vs inactive:3.62 ± 1.76,$P < 0.001$),however, there is a great overlap of SUVmax values between the two sides (Fig. 1.).

Correlation between ratios based on SUVmaxandradioactivity counts.

SUVmax-based ratios between the two sides correlated well with the ratios based on maximum counts ($R = 0.944$,$P < 0.001$) (Fig. 2).

3.3. Comparison of SUVmaxamongsubgroups

All sides of the condyles were comparedwithin the subgroup and among the subgroups (Fig. 3).

The inactive group showed higher SUVmax (5.61 ± 1.95) on the left side than the SUVmax (4.91 ± 1.93) onthe right side ($P = 0.01$). In active groups, significant differences inthe SUVmaxwere also found between the active side and theinactiveside (right active group,5.65 ± 2.24 vs 3.18 ± 1.46,$P < 0.001$; left active group:6.30 ± 2.71vs 4.19 ± 2.00,$P = 0.002$).

Comparing the SUVmax of unilateral side distribution in the inactive group to the ipsilateral side of SUVmaxon theactivecondyles in the active groups showed no significant difference (right side: 4.91 ± 1.93 vs 5.65 ± 2.24,$P = 0.34$; left side: 5.61 ± 1.95 vs 6.30 ± 2.71,$P = 0.49$). When the SUVmax of the inactiveside of condylesinthe active groupscompared with the SUVmaxon the ipsilateral side of the inactive group, there was no significant difference in the right side (active: 4.19 ± 2.00 vs inactive:4.91 ± 1.93,$P = 0.46$), but a significant lower SUVmax in the left inactivesides of active groups than that in the inactive group (3.18 ± 1.46vs5.61 ± 1.95,$P = 0.002$) (Fig. 3).

There is no significant difference when SUVmax of both the activesides wascompared, (right active:5.65 ± 2.24 vs left active:6.30 ± 2.71. $P = 0.39$).

When the SUVmax of both inactivesides of active subgroups was compared, there is no significant difference (right inactive: 3.18 ± 1.46 vs left inactive: 4.19 ± 2.00. $P = 0.17$).

Table 1
Demographics of patients.

	Patient numbers	Gender (female/male)	Age(y) mean ± SD
Normal	11	6/5	19.09 ± 1.04*
Left active	12	7/5	22.17 ± 2.65
Right active	16	10/6	22.18 ± 3.50
Total	39	23/16	21.31 ± 3.03

SD:standard deviation. * Significantly different from affected groups at $P < 0.01$.

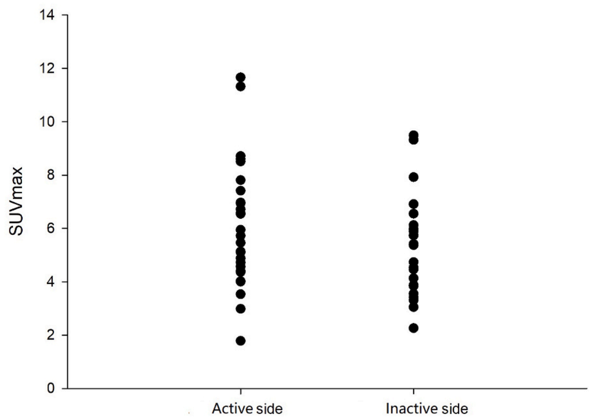

Fig. 1. Distribution of the SUVs on the activeand inactivecondyles.

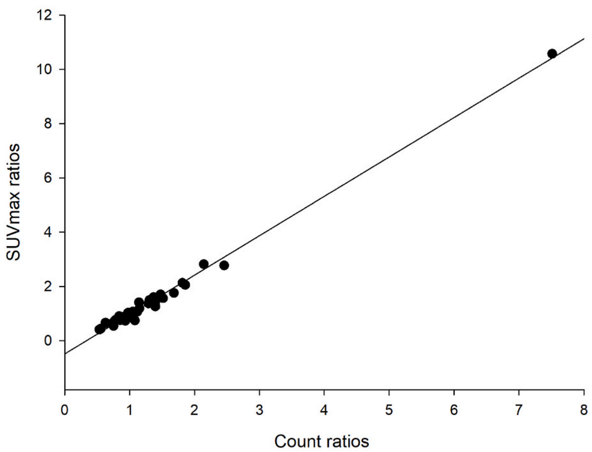

Fig. 2. Correlation between the SUVs and the maximal counts on condyles.

3.4. Receiver operating characteristic (ROC) analysis

The SUVmax value of the active condyles and the inactive condyles of all patientswere used in ROC curve analysis. ROC analysis showed area under the curve (AUC) was 0.588, (P = 0.291,CI:0.428–0.728) (Fig. 4).

In ordertoeliminatebias from the difference of distribution of SUV between both sides of condyles, Further analysis with unilateral condyles wasperformed, the ROC curve analysis using the right active sides and the right inactive sides showed the AUC was 0.606, (P = 0.370,CI:0.373–0.870) (Fig. 5). ROC analysis with the left active sides and the left inactive sides showed AUC was 0.583(P = 0.498, CI 0.343–0.824) (Fig. 6).

The relatively lower areas under the curve mean the SUVmax is not an optimal index to be a diagnostic marker to differentiate active condyles from inactive condyles. Moreover. there wereapparently no meaningful cutoff values to be implemented.

4. Discussion

Our results demonstrate that the semiquantitative parameter SUVmaxwas successfully used in condyles activity assessment (Fig. 7). The SUVmax of the activeside of condyles is significantly higher than that of the inactiveside. SUVmax-based ratios between the two sides correlated well with the ratios based on maximum counts.

SPECT/CT is a recently introduced state-of-the-art modality that enables objective quantitation of radioactive uptake and is documented to be a powerful investigative tool in clinical practice [12]. By using algorithms for CT-based attenuation correction, scatter correction, and resolution recovery. SPECT/CT could generate quantitative imaging voxels denoted as units of radioactivity per volume, then the half-quantitative parameter SUV could be calculated with lesion radioactivity normalized with injected radioactivity and body weight. Excellent accuracy in both phantom (error<3.6 %) and patient (error<1.1 %) was reported.

The female predominance in patients (female:23; male:16) was observed in our study, which is consistent with the previous study that women develop CH significantly more frequently with 64 % (95%CI,58–70 %; n = 275 patients) in a meta-analysis [3]. The

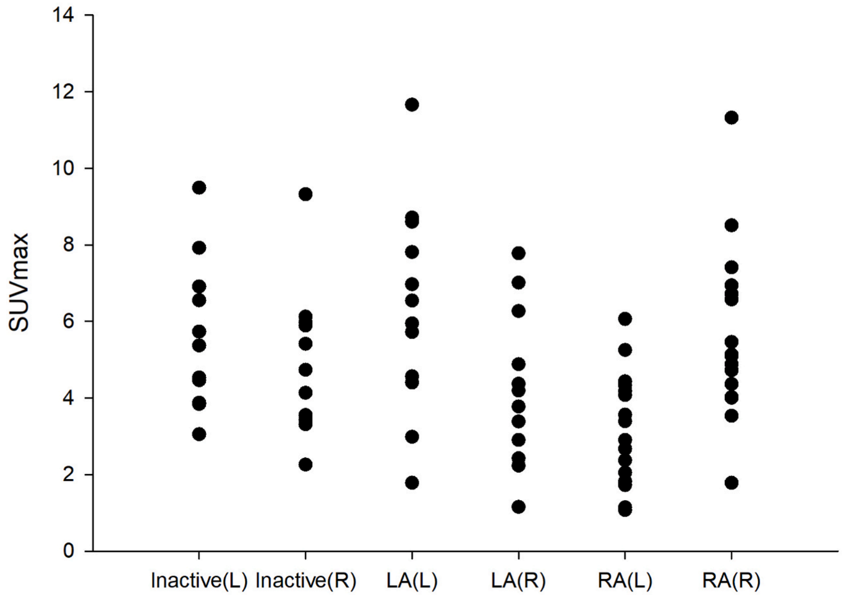

Fig. 3. Distribution of the SUVmax on the sides of condyles among subgroups (L = Left side; R=Right side; LA = Left activeside; RA = Right activeside).

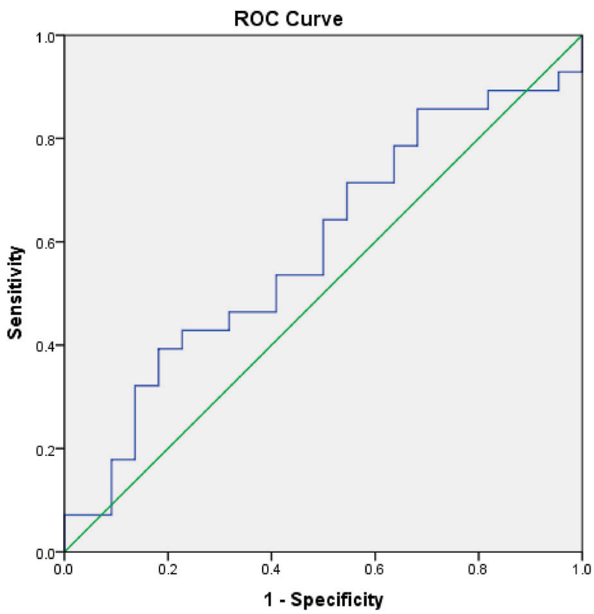

Fig. 4. ROC curve based on theSUVs between the activeand the inactivecondyles.

predominance of right condyles affected was also observed in our study with 16 patients versus 12 patients with left condyles affected. This finding is in concordance with previous studies with a ratio of 3:1 [21].

The significantly higher SUV of activecondyles than that of inactivecondyles is demonstrated in our study, whether the activeside lies on the right side or left side. The result is consistentwithprevious studies [18,22]. One study conducted by Saridin et al. with PET, which showed that the net rate of florid influx (Ki) within the affected condyle was significantly higher than that in the contralateral condyle ($P = 0.018$) [18]. Another study's results also showed the mean bSUVof condyle on the activeside was 15.32 compared with 9.85 on the inactiveside ($P = 0.0007$) [22]. However, no definite cutoff value could be yielded as ROC analysis showed worse diagnostic performance of SUV ($AUC = 0.588$,$P = 0.291$,CI:0.428–0.728).

In the inactive group of UCH patients, the condyles of the left side showed significantly higher SUVmax than the contralateral side (left: 5.61 ± 1.95, right: 4.91 ± 1.93) ($P < 0.01$). The difference was also documented by a study of 32 patients without condyle disease

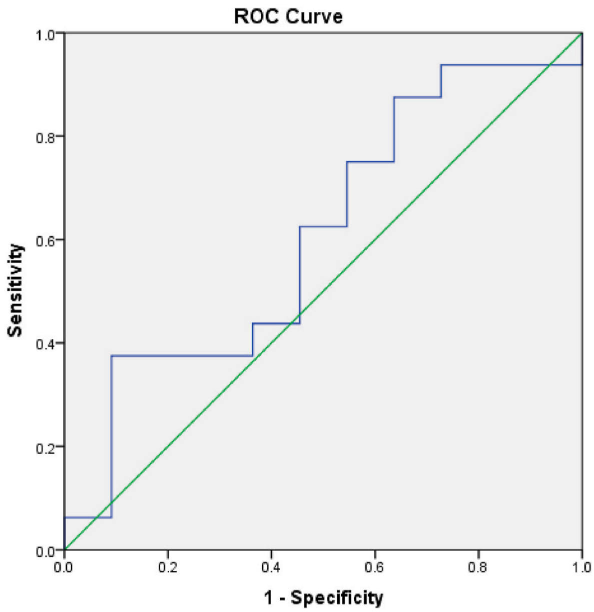

Fig. 5. ROC curve based on the SUVsbetween theactiveand inactivecondyles on the right side.

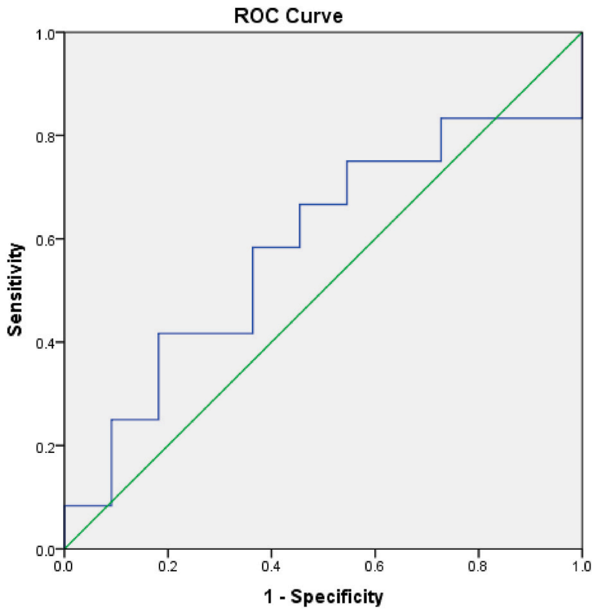

Fig. 6. ROC curve based on the SUVs between activeand inactivecondyles on the left side.

[23]. The study showed a statistically significant difference between the 2D maximum condyle counts of right and left condyles ($P < 0.01$). The left condyle maximum value is 6.7 % higher than the right on average. Nevertheless, the ratio of SUV between condyles is correlated well to the ratio of count ($R = 0.944, P < 0.001$), it suggests that SUV could replace counts per pixel in future quantitative analysis with SPECT/CT.

However, when comparingthe SUVmaxof the activeside condyleswith theipsilateral side condylesinthe inactive group,the SUVmax of the unilateral side of condyles in the inactive group was not significantly different from that of the ipsilateral side of theactivegroup, whether the affected side of condyles was theleft side or the right side. This result was also demonstrated by the study with PETthat the net fluoride uptake (Ki) on the suspected side was equal to that in the normal control subjects ($P = 0.317$) [18]. The results suggest that the affected condyles may be as active as normal condyles in growth,The wide range of SUVmax valueswithin thecondyles and the considerable overlap of SUV values among each side of condyles may also contribute to the insignificance. From our data, the distribution of SUVmaxvalues of each side of condyles overlapped greatly as that shown in Fig. 1. The diversity of data also was

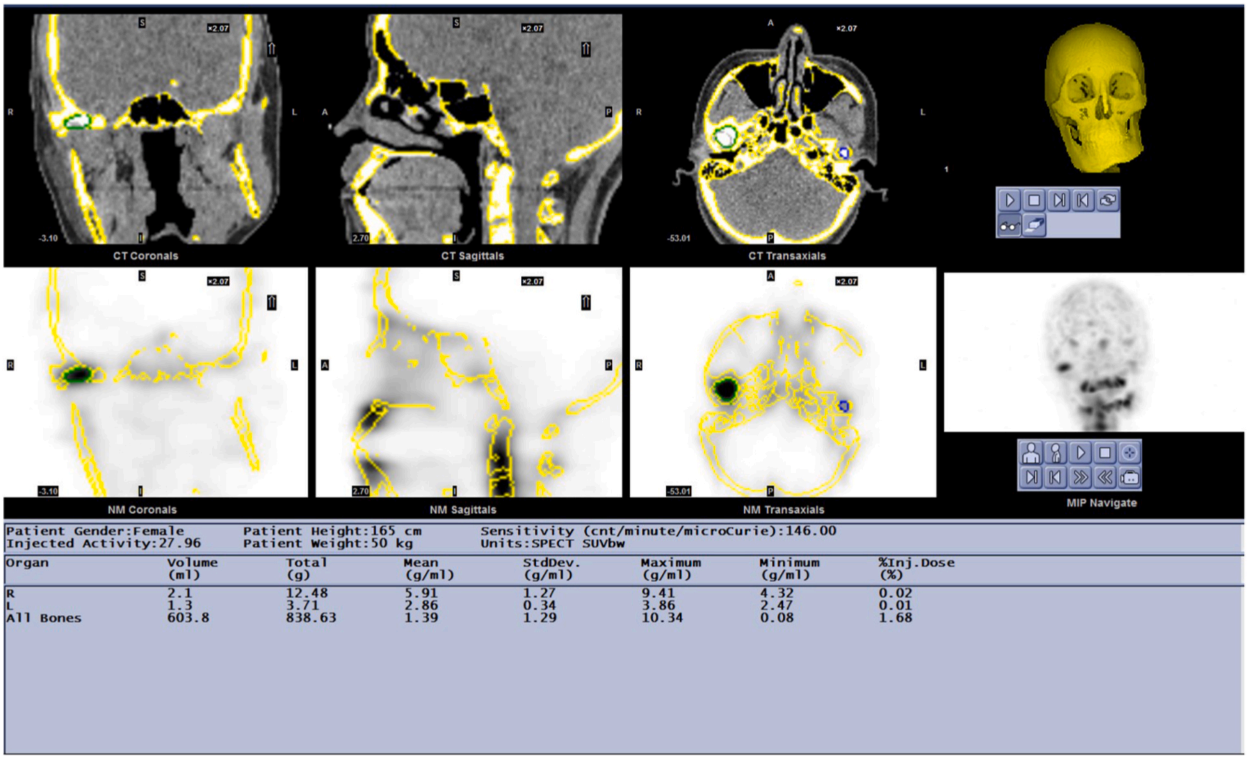

Fig. 7. An example picture of quantitative analysis with SPECT/CT.

demonstrated in studies with 18F-fluoride PET in the assessment of unilateral condylar hyperplasia [16,18]. It is avery interesting finding that the inactiveside of the left condyle in the right active side group showed a significantly lower mean SUVmax value than that of the inactive ratio group, while the right inactiveside showed no significant difference fromthe right side in the inactive group. Based on these observations, and the relatively higher SUV onthe left side than that onthe right side in the inactive ratio group, we speculatedwhether the left condyle may be the culprit inthe development of condylar hyperplasia. When the left side condyle isabnormally less or more active than normal level, itcould cause the relative imbalancein thegrowth of condyles. Further studiesare needed to confirm the hypothesis.

The main limitation of this study is the small subject population and the fact that our data may have a bias for the patients enrolled who were clinically diagnosed with unilateral condylar hyperplasia, normal subjects without UCH were not included. The usefulness of quantitative values with SPECT/CT should be tested with a larger cohort. The other limitation is that our study uses an uptake difference of more than 10 % between condyles on the SPECT as an active UCH standard. Recent studies showed that the SPECT, compared with morphometric analysis, performed poorly with an AUC between 0.53 and 0.65 in diagnosing UCH [10,11]. Further studies with morphologic analysis as a standard are necessary. However, there is no widely accepted gold standard diagnostic method for UCH. Using clinical modalities to determine the cessation of condylar growth requires at least two measurements 6–12 months apart, which may cause unnecessary delay. Quantification by SPECT/CT provides reliable quantification of bone physiologic processes. Combined with condylar histomorphometry measurements, it may improve our insight into the pathophysiology of UCH.

5. Conclusion

SUVs obtained with quantitative SPECT/CT could not provide a definite cutoff value to differentiate active status from the inactive status of condyles due to the wide range of SUV values and considerable overlapamong the sides of condyles. Further studies need to be conducted to elucidate the correlation between SUVs and the pathology underlying the UCH.

Ethical approval

All protocols for this study were approved byapproved by Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine Ethics Committee (Approval No.:SH9H-2023-T198-2)

Data availability statement

Data included in article/supp. material/referenced in article.
No additional information is available for this paper.

Research support

This research received no external financial or non-financial support.

Relationships

There are no additional relationships to disclose.

Patents and intellectual property

There are no patents to disclose.
Other Activities.
There are no additional activities to disclose.

CRediT authorship contribution statement

Pingan Liu: Writing - review & editing, Writing - original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jun Shi:** Writing - original draft, Software, Resources, Methodology, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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