Single Photon Emission Computed Tomography without and with Hybrid Computed Tomography in Mandibular Condylar Hyperplasia

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Objective: *Bone scintigraphy (BS) has been the mainstay in evaluating patients with mandibular condylar hyperplasia (CH). Both planar BS and single photon emission computed tomography (SPECT) have been used to determine cessation of condylar hyperactivity before corrective surgery. The present study aimed to examine the utility of the relatively new single photon emission computed tomography/computed tomography (SPECT/CT) technique for evaluation of CH.*

Material and Method: *Sixty-one mandibular Tc-99m methylene diphosphonate bone SPECT/CT studies were reviewed. Images were analyzed without and with fusion with anatomical CT. Condylar uptake were quantified and differences in uptake between the right and left condyles were determined by both maximum uptake and average uptake in the region of interest (ROI). Differences exceeding 10 percentage points indicated condylar hyperactivity.*

Results: *SPECT and SPECT/CT showed positivity in 34 and 31 examinations, respectively. Agreement between the two modalities was high, but was not perfect. SPECT was found to be more reproducible than SPECT/CT. Quantification using maximum ROI counts was more reproducible than using average ROI counts.*

Conclusion: *No evidence was found to indicate superiority of SPECT/CT over simple SPECT for evaluation of condylar hyperactivity in CH, as demonstrated by the lower intra-modality reproducibility and a trend towards lower sensitivity for detection of hyperactive condyles. Utilization of SPECT alone would further benefit in terms of reduction of patient radiation exposure which is a concern, especially in younger patients such as those with CH. When using quantification, maximum ROI counts should be used over average ROI counts.*

Keywords: *Condylar hyperplasia, Facial deformity, Facial asymmetry, Bone scintigraphy, Single photon emission computed tomography, Radionuclide imaging*

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Condylar hyperplasia (CH) is a rare skeletal malformation characterized by excessive growth of one mandibular condyle[1]. This condition is encountered in adolescence or early adulthood[2]. Facial asymmetry is the most common presentation with patients complaining of chin deviation to the contralateral side of the affected condyle[3]. A number of surgical approaches are available for correction of facial deformities brought on by CH[4]. Bone scintigraphy (BS) has been used to study patients with CH for over three decades[5]. The value of BS in CH lies not only within its ability to diagnose the condition, which is in most cases clinically diagnosed, but also in its predictive power to identify cases which the hyperplastic condyle has become inactive thus defining the appropriate timing of corrective surgery[6]. In the past, activity of the mandibular condyles was assessed using two-dimensional planar BS either by visual analysis[7] or quantification by comparison with reference bony structures[8]. However, with the advent of the three-dimensional single photon emission computed tomography (SPECT) imaging, a more precise quantification of differential uptake in the condyles can be assessed. A difference of greater than 10 percentage points between the two condyles indicates that the condyle with the greater activity is currently still active and surgery should be deferred[3,9,10]. SPECT has been found to be more sensitive for identification of active condyles than planar scintigraphy[7,11].

In recent years, hybrid imaging that

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incorporates the functional information obtained from radionuclide studies with the anatomical information obtained from computed tomography (CT) has become the mainstay of modern Nuclear medicine imaging. The single photon emission tomography/ computed tomography (SPECT/CT) fuses the SPECT image with an anatomical CT image which in theory should help improve precision of quantification of condylar uptake through better anatomical localization and attenuation correction. Characteristics of the condyles can also be assessed in the CT portion of the SPECT/CT. To the authors' best knowledge, there has not been a study that examined the utility of this relatively new imaging modality in patients with CH.

The present study aimed to examine the added value of SPECT/CT over SPECT alone for determination of condylar activity in patients with CH, as well as to determine whether the maximum or average region of interest (ROI) counts should be used for quantification.

Material and Method

Patients

This retrospective study was approved by the institutional review board of Khon Kaen University (reference number HE591122). Patients who underwent mandibular bone SPECT/CT at the authors' institute were identified from the database. Patients who underwent SPECT/CT for reasons other than CH, or were found to have concomitant abnormalities of the temporomandibular joint (TMJ) or mandibular condyles were excluded.

SPECT and SPECT/CT imaging and processing

The patients were intravenously injected with 15 millicuries of Tc-99m methylene diphosphonate. After an uptake time of 3 hours, SPECT/CT of the skull from vertex to chin was acquired using Discovery NM/CT 670 SPECT/CT system (General Electric, NY, USA) equipped with dual-head gamma cameras. The SPECT portion was acquired using LEGP collimator with 128x128 matrix in step and shoot mode for 20 seconds every 3 degrees taking a total imaging time of approximately 20 minutes. The CT portion was acquired using 140 kV, 50 mA, with 2.5 mm slice thickness. Images were processed using the Volumetrix Software included in Xeleris 3 software suite provided by the manufacturer (General Electric, NY, USA). Quantification of condylar activity on SPECT images was done. The axial images were viewed in the French color scale. A circular 13-pixel region of interest (ROI) was placed over each mandibular condyle in the image section which showed the most intense uptake. In cases where identification of the condyle was uncertain in the axial image, further examination of the coronal and sagittal images was done. The maximum ROI count, i.e. the pixel with the highest count, and the average ROI count, i.e. the arithmetic mean of the 13 pixels in the ROI, were recorded. Fig. 1 demonstrates an example of quantitative analysis of SPECT and SPECT/CT images. For the SPECT/CT, quantification was done in the same fashion as with the SPECT images, but the CT map was used to localize the condyles instead of the coronal and sagittal images. Fig. 2 illustrates an example of SPECT/CT imaging.

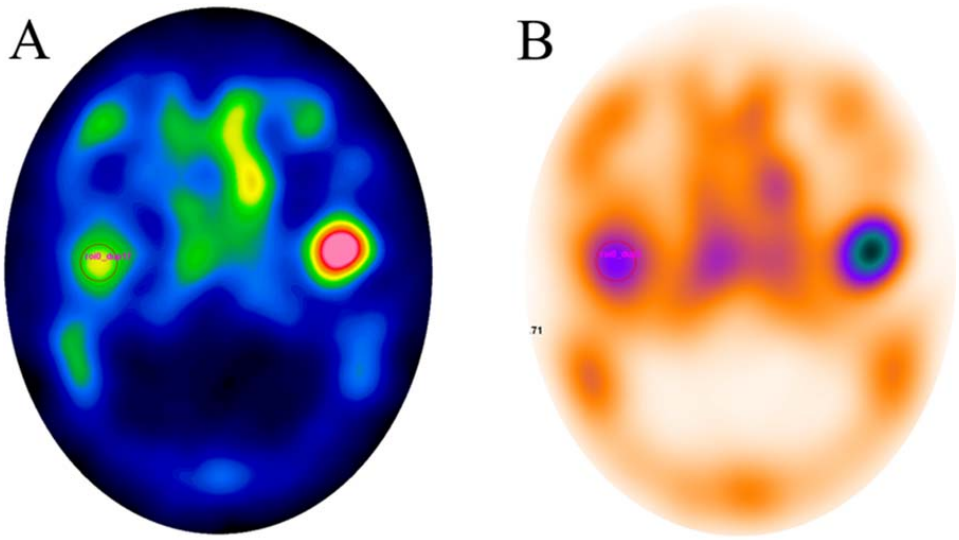
Image analysis and interpretation

Images were analyzed and interpreted by an experienced Nuclear medicine physician for interpretation of mandibular condyle bone scintigraphy studies. In order to determine the degree of activity in the mandibular condyles, ROI counts were used to calculate the differential uptake of each condyle by the following formula.

$$\text{Differential right condylar uptake} = \frac{\text{Right condylar count}}{\text{Right condylar count + Left condylar count}} \times 100$$

$$\text{Differential left condylar uptake} = \frac{\text{Left condylar count}}{\text{Right condylar count + Left condylar count}} \times 100$$

The unit of differential condylar uptake was in "percentage points", which could range from 0-100%, the normal value being approximately 50% for each condyle. Then, the difference of uptake between the condyles was determined by subtracting the differential condylar uptake of the condyle with lesser uptake from the condyle with greater uptake. A difference of uptake greater than 10 percentage points was indicative of hyperactivity in the condyle with greater uptake. The images were then examined for misregistration between the SPECT and CT portions. If the point of maximum uptake in the SPECT images aligned with the center of the condyle in the CT image, the study would be considered to have no misregistrations. If the point of maximum uptake did not align with the center of the condyle, but was still within the condyle, the study would be deemed to have minimal misregistration. If the point of maximum uptake lied outside of the condyle, the study would be considered to have significant misregistration. The 3D volume render of skull from the CT image was examined to assess the severity of facial asymmetry. No facial asymmetry was considered to be present if the tip of the chin was at the midline. Mild asymmetry was defined as cases with just appreciable chin deviation, moderate



	Right	Left		Right	Left
Ave.	205.38	439.007	Ave.	768	1277.692
Max.	249	575	Max.	907	1738

Fig. 1 Quantitation of condylar uptake from SPECT images reconstructed without (A), i.e. SPECT alone, and with anatomical CT (B), i.e. SPECT/CT. Average and maximum counts in ROIs of identical size placed over the most intense part of the right and left condyles were measured. To be noted that counts from SPECT/CT were much greater than from SPECT which was due to attenuation correction made possible by the anatomical CT map.

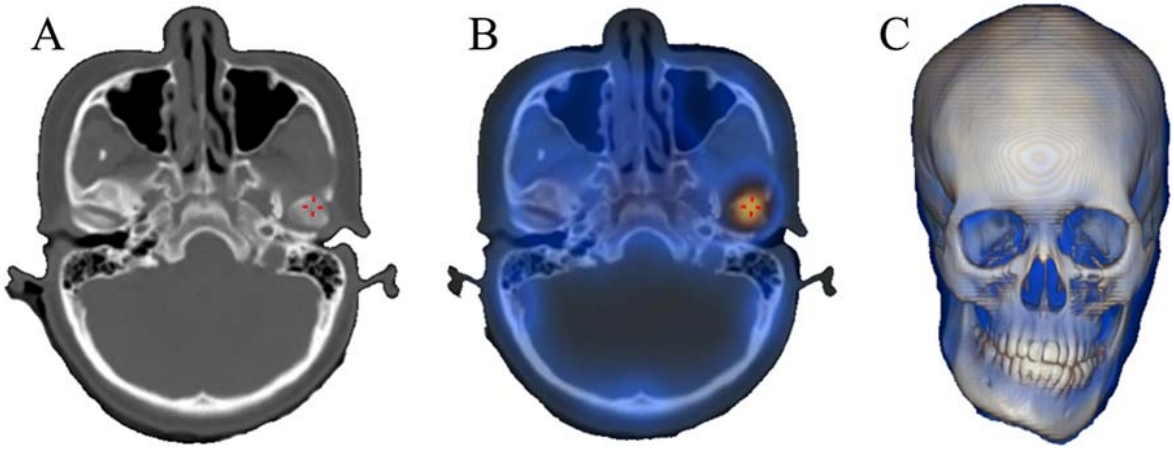


Fig. 2 SPECT/CT of the skull from the same patient as in Fig. 1. Anatomical CT (A) at the level of the mandibular condyles shows enlargement of the left condyle. Fused SPECT/CT (B) shows intense radiopharmaceutical uptake in the left condyle. Three-dimensional CT volume render of the skull shows marked deviation of the chin to the right side. These findings indicate active hyperplasia of the left mandibular condyle.

asymmetry was defined as cases with more readily detectable deviation, and severe asymmetry were cases with striking chin deviation possibly with other abnormalities such as clear elongation of the affected mandibular ramus or malocclusion.

Statistical analysis

Patient characteristics were described as mean, standard deviation, and percentage. Agreement between SPECT, and SPECT/CT results were determined using percent agreement and Cohen's

kappa. McNemar's test was used to compare the positivity fraction between the imaging modalities. Statistical analyses were carried out using Stata 10. A *p*-value of <0.05 was considered to indicate statistical significance.

Results

Patient characteristics

From 1 May 2013 to 31 January 2016, a total of 62 mandibular condyle bone scintigraphy examinations from 52 patients were analyzed at the authors' center. One analysis from a patient that had TMJ ankyloses was excluded leaving a total of 61 examinations from 51 patients being included in the study. Characteristics of included subjects are described in Table 1. The cohort had a slight female predilection, with a mean age of 21.6±3.4 years. The majority of patients had clinically apparent facial asymmetry with only a small proportion that displayed no apparent chin deviation. The severity of facial asymmetry was mostly mild or moderate.

Agreement between SPECT, SPECT/CT, and anatomical CT

Results of the SPECT and SPECT/CT were examined with respect to scan positivity as determined by the differences of quantified condylar uptake of exceeding 10 percentage points, and laterality, i.e. which condyle has greater radiopharmaceutical uptake. As shown in Table 2, when interpreting results using maximum condylar uptake, SPECT and SPECT/CT showed substantial agreement of both positivity (κ = 0.7044) and laterality (κ = 0.8205). However, agreement was only moderate when using average condylar uptake for both positivity (κ = 0.5664) and laterality (κ = 0.5878). Percent agreement was also high with all analysis approaches. It is noteworthy that analysis using maximum rather than average condylar counts yielded better agreement between SPECT and SPECT/CT. On the other hand, when agreement between anatomical CT alone and SPECT results were examined, in terms of positivity, CT alone had only slight to fair correlation with SPECT obtained both without (κ = 0.1555) and with (κ = 0.2469) CT fusion. In terms of laterality, CT alone had substantial agreement with SPECT without (κ = 0.6889) and with (κ = 0.6196) CT fusion. Moreover, CT alone showed appreciable asymmetrical condylar enlargement in only 28 (46%) patients which indicate that CT alone may not be sensitive enough to detect CH.

Table 1. Patient characteristics

Total subjects	61 (100%)
Gender	
Males	25 (41%)
Females	36 (59%)
Age (years ± SD)	21.6±3.4
Facial asymmetry	
Chin deviates to right	25 (41%)
Chin deviates to left	29 (47%)
No apparent deviation	7 (12%)
Severity of facial asymmetry	
No deviation	7 (12%)
Mild	33 (54%)
Moderate	17 (28%)
Severe	4 (6%)

Intra-modality reproducibility

To investigate reproducibility of SPECT and SPECT/CT results, all examinations were analyzed twice and reproducibility was determined. As demonstrated in Table 3, both SPECT and SPECT/CT had almost perfect reproducibility, although SPECT appeared to be superior to SPECT/CT, with perfect agreement (κ = 1.000) for both positivity and laterality. Again, as with inter-modality agreement, it appears that interpretation using maximum counts yielded superior reproducibility than interpretation using average counts. This was true for both SPECT and SPECT/CT.

Description of discrepant cases between SPECT and SPECT/CT

As maximum counts appeared to be superior to average counts in terms of quantification, only cases with discrepancy between SPECT and SPECT/CT based on maximum counts were examined in details. Among the five cases of discrepant laterality, all were classified as negative with differences between condylar uptake of less than 10 percentage points which indicated that these cases had almost equal differential condylar uptake and thus discrepancy in laterality would not be unexpected and did not change the diagnosis in terms of positivity. As outlined in Table 4, of the nine cases with discrepant positivity between SPECT and SPECT/CT, all had concordant laterality. It is noteworthy that on SPECT, six cases were defined as positive and three cases as negative whilst the opposite was true for SPECT/CT. This difference was not statistically significant (p = 0.5078), but the implication of this trend is that if SPECT/CT were used as the diagnostic modality, fewer cases might have been diagnosed as having active condylar growth which could lead to a

Table 2. Agreement between SPECT and SPECT/CT results by quantification of condylar radiopharmaceutical uptake

Positivity*			% agreement	κ	standard error	*p*-value
Maximum count	SPECT/CT		85.25%	0.7044	0.1274	<0.0001
	Positive	Negative				
SPECT						
Positive	28	6				
Negative	3	24				
Average count	SPECT/CT		78.69%	0.5664	0.1221	<0.0001
	Positive	Negative				
SPECT						
Positive	18	11				
Negative	2	30				
Laterality+			% agreement	κ	standard error	*p*-value
Maximum count	SPECT/CT		91.80%	0.8205	0.128	<0.0001
	Right	Left				
SPECT						
Right	37	2				
Left	3	19				
Average count	SPECT/CT		80.33%	0.5878	0.128	<0.0001
	Right	Left				
SPECT						
Right	31	6				
Left	6	18				

* Positivity is defined as the difference between differential condylar uptake of exceeding 10 percentage points.
+ Laterality is defined as the condyle that has the greater activity as quantified by either maximum, or average counts in the region of interest

fraction of patients receiving corrective surgery when their condyles might still be active as defined by SPECT. Comparisons between concordant and discordant cases found that there were no differences between the two groups in terms of age (21.5±3.5 vs. 22.0±2.85, $p = 0.6842$). Using SPECT/CT as the reference, when comparing differences in the degree of condylar uptake, no significant differences were found between the positive cases in the concordant group compared with the discordant group (21.31±11.1 vs. 12.99±2.0 percentage points, *p*-value = 0.2101). This was also true for negative cases where no significant differences were found between the concordant and discordant cases (4.23±2.89 vs. 6.32±2.84 percentage points, *p*-value = 0.1155).

Quality of SPECT and SPECT/CT images

Almost all of the SPECT and SPECT/CT images were assessed as having good quality with only one and two cases being judged as having only fair quality for SPECT/CT and SPECT, respectively. Misregistration, an artifact inherent only to hybrid modalities such as SPECT/CT, proved to be of only minor concern with only 12 (20%) with minimal misregistration and only 3 (5%) with significant misregistration. When compared side-by-side, the SPECT images without and with CT were almost indistinguishable, which suggested that even though

Table 3. Reproducibility of SPECT and SPECT/CT results

	SPECT[++]				SPECT/CT[++]			
	% agreement	κ	standard error	*p*-value	% agreement	κ	standard error	*p*-value
Positivity*								
Maximum count	100.00%	1.0000	0.1280	<0.0001	96.72%	0.9343	0.1278	<0.0001
Average count	90.16%	0.8034	0.1278	<0.0001	91.80%	0.8209	0.1273	<0.0001
Laterality[+]								
Maximum count	100.00%	1.0000	0.1280	<0.0001	100.00%	1.0000	0.1280	<0.0001
Average count	98.36%	0.9654	0.1280	<0.0001	96.72%	0.9313	0.1280	<0.0001

* Positivity is defined as the difference between differential condylar uptake of exceeding 10 percentage points
[+] Laterality is defined as the condyle that has the greater activity as quantified by either maximum or average counts in the region of interest
[++] Both SPECT and SPECT/CT were analyzed twice and reproducibility of results in terms of laterality and positivity were determined for each respective modality

Table 4. Details of the nine cases with discrepant positivity between SPECT and SPECT/CT when quantified by maximum condylar uptake

	SPECT			SPECT/CT	
Positivity	Condylar activity difference	Laterality	Positivity	Condylar activity difference	Laterality
Positive	18.10%	Right	Negative	5.82%	Right
Positive	12.33%	Right	Negative	3.92%	Right
Positive	10.18%	Right	Negative	7.43%	Right
Positive	12.59%	Right	Negative	2.29%	Right
Positive	14.20%	Left	Negative	9.17%	Left
Positive	11.87%	Left	Negative	9.26%	Left
Negative	8.87%	Right	Positive	13.77%	Right
Negative	9.16%	Right	Positive	14.46%	Right
Negative	9.61%	Right	Positive	10.75%	Right

the CT portion of the SPECT/CT was used for attenuation correction, it might not necessarily result in significantly superior SPECT images.

Discussion

The first aim of the present study was to determine the added value of SPECT/CT over SPECT alone for determination of condylar activity in patients with CH. Direct comparison between 61 SPECT and SPECT/CT studies was done to evaluate CH. Age and gender of sample cohort were in concordance with previous studies which reported that CH was a condition of the young and had a slight female preponderance[12]. Among the included patients in the present study, just more than half were identified as having active condyle hyperplasia on either SPECT or SPECT/CT which almost perfectly corresponds with findings from the previous study by Lopez and Corral[11]. The average condylar uptake difference in positive cases was 19.56% for SPECT/CT and 21.02% for SPECT, which was consistent with results from a previous study which found average condylar uptake difference of 18%[13].

The value of SPECT/CT was investigated. First, agreement between the two modalities was compared. As it turns out, the agreement between the

two imaging modalities was high but less than expected. Since SPECT/CT is essentially SPECT imaging with added CT for anatomical correlation and attenuation correction, it was expected that correlation between these two modalities would be near perfect. The discrepant results between the two modalities could be due to a number of factors, but an important factor could lie within CT attenuation correction which, while fast and useful, has the potential to induce quantitative errors[14]. The TMJ and mandibular condyle could be more susceptible to quantitative errors due to its complex anatomy and small size; even minor patient motion causing some misregistration between SPECT and CT images could result in errors.

Secondly, utility of SPECT/CT as hybrid imaging which offers anatomical correlation thus a greater precision in identification of the mandibular condyles should be superior to SPECT. This was also found not to be the case, with SPECT having greater intra-modality reproducibility. As it turns out, localization by SPECT alone was found to be sufficient even in cases where condylar activity was low and inspection of coronal and sagittal images in addition to axial images provided sufficient information for correct localization even without the CT map.

Moreover, when examining only the nine discrepant cases, SPECT was positive in six whilst SPECT/CT was positive in only three which suggested that SPECT may be the more sensitive method for detection of condylar hyperactivity. No differences were found between concordant and discordant cases, in terms of difference in condylar uptake. This is likely due to the fact that the fraction of discordant cases is small compared with concordant cases, so no statistically significant difference was found.

Finally, the benefit exclusive to SPECT/CT, i.e. anatomical information, was scrutinized. The CT portion of the SPECT/CT revealed appreciable condylar enlargement in only about half of the patients. There was only slight to fair agreement between anatomical condylar asymmetry and positivity determined by SPECT or SPECT/CT. Overall, benefits of additional anatomical correlation offered by SPECT/CT seem to be minimal.

The secondary objective of the present study was to determine the better quantification method between use of maximum and average ROI counts. Results showed that maximum ROI counts were superior to average ROI counts as determined by its greater reproducibility. These findings were expected since identification of the pixel with maximum uptake was less prone to error from ROI placement than the average values of all pixels in a certain ROI.

Limitations of the present study were its retrospective nature so patient's follow-ups were not possible. Further longitudinal studies should provide insight to the outcomes of patients with CH evaluated by these two imaging modalities.

Conclusion

No evidence was found to indicate that SPECT/CT is superior to SPECT for evaluation of condylar hyperactivity in CH, as demonstrated by the lower intra-modality reproducibility, a trend towards lower sensitivity for detection of hyperactive condyles, and only moderate correlation between anatomical CT and SPECT findings. Utilization of SPECT alone would further benefit in terms of reduction of patient radiation exposure which is a concern, especially in younger patients such as those with CH. When quantification is used for evaluation of CH, maximum ROI counts should be used rather than average ROI counts.

What is already known on this topic?

Nuclear medicine bone scintigraphy has been the mainstay of evaluation of patients with CH, advancement in imaging equipment and reconstruction permits tomographic imaging (SPECT) which offers superior quantification capabilities over traditional planar bone scintigraphy. Differences in condylar radiopharmaceutical uptake exceeding 10 percentage points indicate active hyperplasia of the affected condyle and further indicate that corrective surgery should not yet be performed.

What this study adds?

To the authors' best knowledge, this is the first study in published literature to examine the utility of SPECT/CT which incorporates anatomical imaging for evaluation of CH. Results show that despite the anatomical information provided by the CT portion of the SPECT/CT, this imaging modality was not found to be superior to simple SPECT for evaluation of CH. From the present evidence, SPECT/CT cannot be recommended over SPECT due to unproven superiority and the burden of added radiation exposure.

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Potential conflicts of interest

None.

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ภาพวินิจฉัยตัดขวางสามมิติคอมพิวเตอร์จากการปลดปล่อยโฟตอนเดี่ยวโดยไม่มีและมีภาพเอกซเรย์คอมพิวเตอร์ร่วมในภาวะส่วนคอนดายล์ของกระดูกขากรรไกรล่างเจริญเกิน

ดริส ธีระกุลพิศุทธิ์, จรูญศักดิ์ สมบูรณ์พร, นันทพร วงศ์สุรวัฒน์

วัตถุประสงค์: การสแกนกระดูก (bone scintigraphy: BS) เป็นการตรวจที่สำคัญในการประเมินผู้ป่วยที่มีภาวะส่วนคอนดายล์ของกระดูกขากรรไกรล่างเจริญเกิน (mandibular condylar hyperplasia: CH) การตรวจ BS แบบแนบระนาบ (planar BS) และแบบสามมิติ (single photon emission computed tomography: SPECT) ใช้ประเมินการหยุดเจริญเกินของกระดูกส่วนคอนดายล์ก่อนที่จะดำเนินการผ่าตัดเพื่อแก้ไขความผิดปกติ การศึกษาปัจจุบันมีวัตถุประสงค์เพื่อประเมินประโยชน์ของการตรวจชนิดใหม่คือการสแกนแบบสามมิติร่วมกับเอกซเรย์คอมพิวเตอร์ (single photon emission computed tomography/computed tomography: SPECT/CT) สำหรับประเมินภาวะ CH

วัสดุและวิธีการ: จากการตรวจ SPECT/CT ของกระดูกขากรรไกรล่าง โดยสารเภสัชรังสีเทคนิเชียม-99เอ็ม เมธิลีนไดฟอสโฟเนตจำนวน 61 การตรวจได้ทำการวิเคราะห์ภาพ SPECT โดยที่ไม่มีและมีเอกซเรย์คอมพิวเตอร์ (CT) ร่วมด้วย โดยวัดปริมาณการจับสารเภสัชรังสีในคอนดายล์ข้างขวาและซ้าย โดยวัดทั้งค่านับวัดสูงสุดและค่านับวัดเฉลี่ยในขอบเขตที่สนใจหากพบว่าความแตกต่างระหว่างคอนดายล์เกิน 10 หน่วยร้อยละ ถือว่ายังมีการเจริญมากของคอนดายล์

ผลการศึกษา: SPECT และ SPECT/CT ให้ผลบวกใน 34 และ 31 การตรวจ ตามลำดับ การตรวจทั้งสองชนิดมีค่าความเห็นพ้องในระดับสูง แต่ไม่ถึงกับสมบูรณ์พบว่า SPECT เป็นการตรวจที่มีคุณสมบัติการทำซ้ำที่ดีกว่า SPECT/CT และการวัดการจับสารเภสัชรังสีโดยใช้ค่านับวัดสูงสุด มีคุณสมบัติการทำซ้ำดีกว่าการใช้ค่านับวัดเฉลี่ย

สรุป: จากการศึกษาปัจจุบันไม่พบหลักฐานว่า SPECT/CT เหนือกว่า SPECT ในการประเมินผู้ป่วย CH โดยพิจารณาจากการที่ SPECT/CT มีคุณสมบัติการทำซ้ำต่ำกว่าและมีแนวโน้มที่จะตรวจจับผู้ป่วยที่ยังมีการเจริญของคอนดายล์อยู่ได้น้อยกว่า SPECT การใช้ SPECT เพียงอย่างเดียวมีข้อดีอีกประการคือปริมาณรังสีที่ผู้ป่วยได้รับมีน้อยกว่า SPECT/CT ซึ่งเป็นข้อควรระวังที่สำคัญโดยเฉพาะผู้ป่วยอายุน้อยดังเช่นผู้ป่วยที่มี CH และหากแปลผลโดยการวัดปริมาณการจับสารเภสัชรังสีในคอนดายล์ การใช้ค่านับวัดสูงสุดดีกว่าการใช้ค่านับวัดเฉลี่ย