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Evaluation of 99mTc Uptake in the Mandibular Condyle, Comparison Between the Two Sides, and Correlation with the First Cervical Vertebra in Patients with Mandibular Deviation

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ABSTRACT

Introduction: This pilot study aimed to evaluate the uptake of the radiopharmaceutical 99mTc in the mandibular condyles and cervical vertebrae on bone scintigraphy and to assess the correlation between inter-condylar metabolic disparities and longitudinal soft-tissue changes in patients presenting with progressive mandibular deviation.

Materials and Methods: This prospective longitudinal pilot study enrolled patients referred to orthodontic and oral and maxillofacial surgery clinics with suspected condylar hyperactivity and mandibular deviation. Bone scintigraphy was performed at baseline to assess 99mTc-MDP uptake in both mandibular condyles normalized against the first cervical vertebra (C1). Standardized facial photographs were obtained at baseline and after a 6-month prospective follow-up period to evaluate soft-tissue asymmetry changes.

Results: Over the 6-month observation period, the most pronounced soft-tissue variations were observed in An.b (mean: 62.40 ± 33.69) and Gn.a (mean: 38.59 ± 34.41). Bivariate Pearson correlation analysis revealed a statistically significant, strong negative correlation between inter-condylar 99mTc uptake differences (L–R) and changes in pog.oc (r = -0.821, 95% CI: [-0.96, -0.26], p = 0.012). Non-significant moderate-to-strong correlations with inter-condylar uptake differences were noted for Gn.b (r = -0.643, p = 0.086), ph.b (r = 0.607, p = 0.110), and pog.b (r = 0.571, p = 0.139).

Conclusion: Preliminary findings suggest that quantitative 99m Tc bone scintigraphy demonstrated preliminary correlations with specific regional soft-tissue changes. Given the small sample size and lack of diagnostic validation against a reference standard, these findings reflect exploratory associations rather than predictive capability. Larger prospective studies are required to clarify the clinical utility of semi-quantitative scintigraphy in asymmetry management.

Keywords: Mandibular condyle; Condylar hyperactivity; Bone scintigraphy; Technetium 99mTc medronate; Facial asymmetry.

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Introduction

The mandibular condyle is a crucial anatomical and functional component of the temporomandibular joint (TMJ), playing a pivotal role in craniofacial growth, masticatory biomechanics, and the maintenance of stable dental occlusion [1,2]. Due to its unique multidirectional adaptive capacity, condylar morphology and volume dynamically remodel in response to biomechanical forces, functional demands, and systemic or local stimuli [3,4]. Disruption of this biological equilibrium by intrinsic growth anomalies, trauma, or degenerative pathology can alter mandibular architecture, frequently manifesting as progressive skeletal discrepancies and transverse or vertical facial deformities [5,6].

Among the non-neoplastic conditions affecting the TMJ, unilateral condylar hyperplasia (UCH) represents an intriguing developmental disorder characterized by disproportionate, excessive bone proliferation within one condylar process [7]. The underlying active osteoblastic hypermetabolism triggers progressive three-dimensional deformities, such as hemi-mandibular elongation or hyperplasia. which displace the mandibular basal arch, induce dental compensatory changes, and alter adjacent soft-tissue tension [8]. Consequently, affected patients present with progressive chin deviation, severe facial asymmetry, and secondary canting of the occlusal plane, creating significant challenges in therapeutic decision-making and surgical planning [9,10].

Accurate discrimination between active, ongoing condylar hyperactivity and stabilized (quiescent) structural deformity is critical [7,11]. Premature orthognathic intervention during active condylar growth inevitably leads to secondary relapse and progressive skeletal asymmetry, whereas unnecessary delay in quiescent cases prolongs patient morbidity and functional impairment [7,12]. Historically, condylar morphology has been tracked using serial two-dimensional radiographs, including panoramic images and lateral cephalograms [1,13]. However, 2D modalities suffer from inherent projective distortions, anatomical superimpositions, and geometric magnification errors, while lacking the sensitivity to capture real-time cellular activity [2,14]. Although cone-beam computed tomography (CBCT) provides outstanding three-dimensional structural resolution for volumetric assessment, it remains a purely static morphological tool unable to differentiate active metabolic bone remodeling from stabilized skeletal disproportion [15-17].

Single-photon emission computed tomography (SPECT) using technetium-99m methylene diphosphonate (99mTc-MDP) has emerged as the established imaging modality for evaluating regional bone turnover and osteoblastic metabolism [11,18]. By capturing radiotracer incorporation into active osteogenic areas, quantitative and semi-quantitative SPECT metrics allow objective assessment of inter-condylar metabolic disparities [18,19]. However, while the relationship between scintigraphic uptake and osseous morphological changes has been widely documented, the degree to which asymmetrical condylar hypermetabolism reflects in progressive, longitudinal soft-tissue variations remains poorly defined. Facial soft tissues possess dynamic masking, muscular adaptation, and subcutaneous buffering capacities that may not linearly mirror underlying skeletal shifts [20,21]. Therefore, this prospective pilot study aimed to evaluate semi-quantitative 99mTc-MDP uptake in the mandibular condyles normalized against the first cervical vertebra (C1), assess contralateral uptake disparities, and investigate their direct correlation with longitudinal 6-month facial soft-tissue changes in patients presenting with progressive mandibular deviation.

Materials and Methods

This prospective longitudinal pilot study enrolled consecutive patients referred to the oral and maxillofacial surgery and orthodontic clinics of Kermanshah University of Medical Sciences between 2/2025 and 8/2025. The institutional ethics committee approved the study protocol, and all participants provided written informed consent prior to enrollment. All baseline clinical photographs and scintigraphic assessments were performed prospectively upon study entry, and patients were subsequently followed for a 6-month interval to record longitudinal soft-tissue variations. Eligible candidates were scheduled for orthognathic surgery and presented with facial asymmetry, mandibular deviation, or chin deviation as their chief complaint. We excluded patients with prior orthognathic surgery, active orthodontic treatment affecting facial soft tissues, previous maxillofacial trauma, craniofacial syndromes, or systemic bone and metabolic disorders. Temporomandibular joint (TMJ) pathology was assessed during screening; patients with maximum mouth opening below 40 mm or symptoms of internal derangement were excluded. Frontal and profile facial photographs were obtained using a 51-megapixel digital camera (8688 × 5792 pixels, 72 dpi; Canon Inc., Tokyo, Japan) equipped with an external flash unit (Canon Speed lite 600EX II) positioned 200 cm from the

patient. Subjects were seated in Natural Head Position (NHP), achieved by having them look into their own pupils in an eye-level mirror, with the mandible in centric occlusion and lips relaxed. A standardized 10-cm reference calibration ruler (100 mm subdivisions) was placed adjacent to the patient's face within the same focal plane to calibrate digital magnification.

Soft tissue facial landmarks and reference axes were defined on the standardized photographs as follows:

- Reference Axis a (Horizontal): interpupillary line connecting the right and left pupils (Pu).
- Reference Axis b (Vertical): facial midline passing through soft tissue Nasion (Na) perpendicular to axis a.
- Soft tissue Nasion (Na): deepest point of the nasal bridge.
- Subnasale (Sn): midpoint of the columella base angle.
- Soft tissue Pogonion (Pog): most anterior midpoint of the soft tissue chin.
- Nasal Tip (Nt): most prominent point of the nasal apex.
- Oral Commissure (OC): point at the labial commissure.
- Alare (An): most lateral point on the alar contour
- Gonion (Gn): most lateral/inferior point at the mandibular angle.
- Philtrum (Ph): vertical groove at the midline of the upper lip.
- Midline of Teeth (Mt): dental midline between the central incisors (evaluated separately for maxilla [Mt. max] and mandible [Mt.man]).

All linear soft-tissue measurements and bilateral landmark distances were evaluated using a digital caliper calibrated against the 10-cm reference scale. For bilateral structures, the Asymmetry Index (AI) was calculated as:

$$\text{Asymmetry Index (\%)} = [\ |R - L| / (R + L)\ ] \times 100$$

where R and L represent right- and left-side measurements, respectively. Skeletal scintigraphy was performed following intravenous administration of 20 mCi (740 MBq) Technetium-99m Methylene Diphosphonate (99mTc-MDP). After a 3-hour interval to allow radiotracer clearance from soft tissues and binding to metabolically active bone, planar and single-photon emission computed tomography (SPECT) images were acquired using a dual/single-head gamma camera (ADAC-Philips, 2013). Planar views of the skull and facial skeleton were obtained first for spatial orientation, followed by SPECT acquisition using 360-degree rotation and a 128 × 128 matrix. Semi-quantitative analysis of radiotracer uptake was performed on reconstructed transaxial and coronal slices. Circular regions of interest (ROIs) were manually drawn over the active growth centers of the right and left mandibular condyles. An identical ROI was placed over the posterior arch of the first cervical vertebra (C1), which served as the neutral reference site. Total counts within each condylar ROI were recorded and normalized to the C1 reference to calculate the condyle-to-C1 uptake ratio:

Relative Condylar Uptake = Condyle ROI Counts / C1 Reference ROI Counts.

Inter-condylar uptake differences and normalized values were subsequently correlated with soft-tissue asymmetry indices and clinical changes observed between baseline and 6-month follow-up.

Statistical Analysis

Data were analyzed using SPSS software (version 26.0; SPSS Inc., Chicago, IL, USA). Longitudinal soft-tissue changes over the 6-month observation interval were computed as algebraic differences between follow-up and baseline measurements (Δ="Follow-up"-"Baseline"). Continuous variables were summarized using descriptive statistics, including mean, standard deviation (SD), median, and range (minimum and maximum). Bivariate relationships between inter-condylar differences in 99m Tc uptake and 6-month changes in facial asymmetry indices were evaluated using the Pearson correlation coefficient (r). Two-tailed p-values and 95% confidence intervals (95% CI) were calculated for all correlation coefficients, with statistical significance set at $p < 0.05$. One variable (max.mt.b) was excluded from bivariate correlation analysis due to lack of variance (constant values of zero across all subjects). Given the preliminary and exploratory nature of this pilot study (n = 8), adjustments for multiple testing (such as Bonferroni correction) were not applied to avoid inflating Type II error rates; however, all findings are reported transparently with exact p-values and interpreted conservatively.

Results

A total of eight participants were prospectively

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evaluated at baseline and after a 6-month interval to assess changes in facial soft-tissue asymmetry parameters and bilateral condylar 99mTc uptake. The study cohort comprised five female (62.5%) and three male (37.5%) patients, with an overall mean age of 25.00 ± 2.67years (range: 22–29 years). Mandibular deviation involved the left side in four patients (50.0%) and the right side in four patients (50.0%). Regarding baseline clinical severity, five patients (62.5%) exhibited moderate asymmetry, and three patients (37.5%) presented with severe deviation. Individual and summary demographic and baseline clinical characteristics are presented in (Table 1). Descriptive statistics for the 6-month longitudinal changes in facial soft-tissue asymmetry indices and condylar radiopharmaceutical uptake are summarized in (Table 2). The largest mean soft-tissue alterations over the 6-month period were observed in An.b ("mean":62.40 ± 33.69), Gn.a ("mean":38.59 ± 34.41), and An.a ("mean":22.81 ± 22.96). In contrast, the smallest absolute variations were found in pog.b ("mean":-0.09 ± 2.79), ph.b ("mean":-0.06 ± 0.58), and max.mt.b ("mean":0.00 ± 0.00). For the parameter max. mt.b (maxillary dental midline to facial vertical axis b), all participants presented with zero variance across baseline and follow-up evaluations due to the absence of dental midline deviation; therefore, correlation coefficients could not be mathematically computed for this index. Bivariate associations between inter-condylar 99m Tc uptake differences (Left minus Right) and 6-month changes in facial asymmetry parameters were assessed using Pearson correlation analysis (Table 3). A statistically significant, strong negative correlation was observed exclusively for pog.oc (r = -0.821, 95%" CI " [-0.96-0.26], p = 0.012). Although notable correlation coefficients were noted for Gn.b (r = -0.643, p = 0.086), ph.b (r = 0.607, p = 0.110), and pog.b (r = 0.571, p = 0.139), they did not reach statistical significance (p ≥ 0.05).

Table 1. Baseline demographic and clinical characteristics of the study cohort (n = 8).

Patient	*Age (years)*	*Sex*	*Side of mandibular deviation*	*Baseline clinical severity*
1	*28*	*Female*	*Left*	*Moderate*
2	*25*	*Female*	*Left*	*Severe*
3	*23*	*Female*	*Right*	*Moderate*
4	*24*	*Male*	*Right*	*Moderate*
5	*29*	*Male*	*Left*	*Severe*
6	*22*	*Male*	*Right*	*Moderate*
7	*23*	*Female*	*Right*	*Moderate*
8	*26*	*Female*	*Left*	*Severe*
Overall Summary	*25.0 ± 2.6*	*F (62.5%) M (37.5%)*	*Left (50.0%) Right (50.0%)*	*Moderate (62.5%) Severe (37.5%)*

Table 2. Descriptive statistics of 6-month changes in soft-tissue asymmetry indices and 99mTc condylar uptake (n = 8).

B Parameter	*Mean*	*SD*	*Median*	*Minimum*	*Maximum*
Sn.a	*1.13*	*2.21*	*1.42*	*-3.46*	*3.51*
Sn.b	*-0.24*	*0.11*	*-0.24*	*-0.39*	*-0.12*
pog.a	*4.22*	*4.97*	*4.11*	*-1.23*	*11.18*
pog.b	*-0.09*	*2.79*	*0.59*	*-3.70*	*3.90*
Nt.b	*0.21*	*0.25*	*0.18*	*0.00*	*0.68*
Nt.a	*0.88*	*1.36*	*0.00*	*-0.37*	*3.22*
An.a	*22.81*	*22.96*	*19.27*	*2.24*	*64.28*
An.b	*62.40*	*33.69*	*60.00*	*4.30*	*95.65*

SD: Standard Deviation; L: Left condyle; R: Right condyle; L–R: Inter-condylar uptake difference (Left minus Right).

Table 3. Pearson correlation coefficients between inter-condylar ^{99m} Tc uptake differences (L–R) and changes in facial asymmetry indices.

Index	*Pearson correlation (r)*	*95% Confidence Interval*	*p-value*
pog.oc	*-0.821*	*[-0.96, -0.26]*	*0.012**
Gn.b	*-0.643*	*[-0.92, 0.10]*	*0.086*
ph.b	*0.607*	*[-0.16, 0.91]*	*0.110*
pog.b	*0.571*	*[-0.21, 0.90]*	*0.139*
Gn.a	*0.321*	*[-0.48, 0.82]*	*0.438*
Sn.b	*0.286*	*[-0.51, 0.81]*	*0.493*
Nt.b	*0.252*	*[-0.53, 0.79]*	*0.547*
man.Mt.b	*0.179*	*[-0.58, 0.76]*	*0.672*
An.b	*-0.143*	*[-0.75, 0.60]*	*0.736*
Nt.a	*-0.107*	*[-0.73, 0.62]*	*0.801*
pog.a	*-0.107*	*[-0.73, 0.62]*	*0.801*
Sn.a	*-0.107*	*[-0.73, 0.62]*	*0.801*
An.a	*0.036*	*[-0.67, 0.70]*	*0.933*
ph.a	*-0.029*	*[-0.70, 0.67]*	*0.946*

* Statistically significant at $p < 0.05$. Note: max.mt.b was excluded from the correlation analysis due to constant values across all participants (variance = 0).

Discussion

Mandibular condylar remodeling plays a pivotal role in orthodontic and orthognathic surgical planning. In patients presenting with progressive facial asymmetry, discriminating between active hyperplastic bone growth and stable anatomical asymmetry is critical for determining surgical timing [7,10]. In the current pilot study, we evaluated the correlation between inter-condylar 99mTc-MDP uptake disparities and 6-month longitudinal soft-tissue asymmetry alterations. A critical methodological aspect of scintigraphic quantification in the maxillofacial region is the selection of a reliable neutral reference standard. In our protocol, the posterior arch of the first cervical vertebra (C1) was utilized as the reference standard for normalizing condylar counts.

The C1 vertebra offers key methodological advantages over alternative reference sites: it is consistently captured within the same field of view as the temporomandibular joints, ensuring identical physical attenuation and acquisition geometry [19,22]. Furthermore, unlike facial skeletal structures that frequently undergo secondary compensatory remodeling in asymmetric conditions, C1 maintains metabolic stability and is unaffected by mandibular biomechanics or dental malocclusion [2,19]. Normalization against C1 accounts for individual variability in radiopharmaceutical clearance, body mass index, and background tissue vascularity, aligning with standardized semi-quantitative nuclear imaging protocols [19]. Regarding soft-tissue changes, the most pronounced variations over the 6-month interval were observed in mandibular and alar parameters (An.b, Gn.a, and An.a). Bivariate correlation analysis revealed a statistically significant inverse correlation between inter-condylar uptake differences and pogonion deviation relative to the occlusal reference line (pog.oc: $r = -0.821$, $p = 0.012$).

Furthermore, moderate-to-strong non-significant correlation coefficients were noted for Gn.b ($r = -0.643$), ph.b ($r = 0.607$), and pog.b ($r = 0.571$). These findings are consistent with biomechanical models showing that localized asymmetric condylar hyperactivity predominantly affects the lower facial third, projecting translational vectors toward the gnathion and pogonion [8,23]. In comparison with previous literature, our observations corroborate the work of López et al. [19], who demonstrated that inter-condylar uptake disparities on 99mTc-MDP SPECT correlate with progressive facial asymmetry. However, while earlier investigations by Heider et al. [22] and Wen et al. [24] emphasized the diagnostic value of SPECT/CT in anatomical and hard-tissue localization, our study focused specifically on dynamic soft-tissue changes. Notably,

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while skeletal deviation directly mirrors condylar hypermetabolism, soft-tissue responses are frequently mitigated or confounded by masticatory muscle compensation and variable subcutaneous tissue thickness [20,21]. Thisphysiological buffering may explain why several lateral facial variables did not achieve formal statistical significance.

Limitations

Several limitations of this study should be highlighted. First, the small sample size (n = 8) inherently limits statistical power, increases the probability of Type II errors, and precludes multivariable regression modeling or formal diagnostic accuracy validation, such as ROC analysis. Second, the 6-month follow-up window represents a relatively short period for detecting substantial soft-tissue remodeling. Third, facial changes were monitored using calibrated two-dimensional photography rather than serial three-dimensional CBCT voxel-based superimposition, preventing direct volumetric hard-to-soft tissue registration. Fourth, the absence of a healthy control group limited direct comparison with normognathic individuals. Fifth, recruitment from a single academic referral center may have introduced potential selection bias and may limit the generalizability of the findings. Therefore, these results should be interpreted strictly as preliminary exploratory findings.

Conclusion

The results of this pilot study provide preliminary observations regarding the correlation between inter-condylar 99mTc radiopharmaceutical uptake differences and 6-month soft-tissue asymmetry changes in patients presenting with mandibular deviation. Although bivariate associations were observed, notably between inter-condylar uptake differences and pogonion deviation relative to the occlusal reference line (pog.oc), these findings do not establish predictive validity, nor do they support predicting future skeletal growth without formal diagnostic accuracy metrics (such as sensitivity and specificity) validated against a reference standard. Rather, semi-quantitative scintigraphy in this context serves as an adjunctive, exploratory tool for characterizing condylar metabolic patterns. Adequately powered prospective longitudinal investigations are warranted to determine whether these scintigraphic metrics hold definitive prognostic value in clinical treatment planning.

Conflict of Interest

There is no conflict of interest to declare.

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