# Investigation of the Impact of Insulin Resistance on the Bone Density of the Upper Wall of the Maxillary Sinus

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**Abstract**

The aim of our study was to investigate the impact of insulin resistance on the bone density of the upper wall of the maxillary sinus. Materials and Methods: The study included 100 female participants aged 18 to 44 years, divided into two groups. The first group consisted of individuals with insulin resistance, while the control group comprised individuals without signs of insulin resistance. In each group, we conducted an investigation of the radiological density of the upper wall of the maxillary sinus using uncertainty calculations. Results of the study suggest a potential influence of insulin resistance on the density of bone tissue around the nasal sinuses, specifically the upper wall of the maxillary sinus in our case. This parameter was found to be minimal in the group of individuals with insulin resistance. It is particularly noteworthy that both minimum and maximum bone density decreased in this group. Conclusions. The research focused on how insulin resistance affects the density of the upper wall of the maxillary sinus. By employing uncertainty calculations, the study revealed that insulin resistance is associated with a decrease in the minimum density of the upper wall of the maxillary sinus. This tendency may act as a catalyst for the emergence of significant inflammatory alterations in the nasal sinuses, serving as a foundation for the initiation of complications.

**Keywords** [1]

Bone density, multispiral computer tomography, uncertainty, paranasal sinuses, resistance to insulin

## 1. Introduction

To this day density is one of the main indicators of bone structure. In most cases, both scientists and practicing doctors focus on the density of long tubular bones with the aim of determining the degree of osteoporosis [1]. Research methods used to measure density, most commonly dual-energy X-ray absorptiometry [2] (DEXA), involve additional time and the participation of additional medical personnel, making this method economically unfeasible, although it is considered the "gold standard" for osteoporosis diagnosis.

Only little work has been dedicated to determine the density of skull bones, which are composed of cancellous bone tissue [3, 4]. This is likely due to the complexity and diversity of the structure of this type of bone tissue, which, unlike compact bone tissue with a structural-functional unit called an osteon, consists of trabeculae and the trabecular space [5]. The presence of a branched system of trabeculae and the interspace between can create additional difficulties in measuring the density of skull bone tissue.

ProfIT AI 2023: 3rd International Workshop of IT-professionals on Artificial Intelligence (ProfIT AI 2023), November 20–22, 2023, Waterloo, Canada

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One of the simplest methods for measuring bone density is the radiological method (often computed tomography, less frequently magnetic resonance imaging) [6]. Radiological research methods can accurately and effectively determine the bone density of any area of the human skull in both healthy physiological and pathological conditions. However, the majority of studies focus on the physiological state or investigate radiological density in the presence of tooth and jaw pathology, particularly the alveolar process of the upper jaw [7, 8].

At present, only isolated studies exist that address density in other pathological conditions in humans. One such pathology deserving special attention from the medical community is insulin resistance.

Insulin resistance is often a marker of metabolic syndrome, affecting around 100 million people according to various sources [9, 10]. It is characterized by cells in the human body becoming insensitive to the action of insulin, disrupting the entry of glucose into cells and leading to a range of pathological processes. There is a hypothesis regarding the connection between insulin resistance and chronic inflammatory processes, which could further worsen the course of various diseases.

Considering the above, the **aim of our study** was to investigate the impact of insulin resistance on the bone density of the upper wall of the maxillary sinus.

## 2. Material and Methods

The study included 100 female subjects aged 18 to 44 years. Although the risk of insulin resistance is comparatively lower in this age group than in middle age, this age range was deliberately chosen to exclude the influence of other factors on bone tissue (such as hormonal changes during menopause). All women underwent CT scans due to non-ENT-related pathology (suspected strokes, unconfirmed cranial bone injuries, etc.). The study was approved by the bioethics committee of Kharkiv National Medical University (protocol No. 1 dated 08.11.2018).

The research was conducted at the Clinical Institute of Emergency Surgery, Kharkiv, based on the existing collaboration agreement with the Kharkiv National Medical University. CT scans were performed on a Toshiba Aquilion-64 spiral computed tomography scanner which is considered the only true volumetric 64-slice CT scanner with 64 detector channels, 3-D cone beam algorithms and volume reconstruction on the market. Automated features in the scanner's SUREWorkflow software enable the operator to monitor a patient's heart rate prior to scanning.

Toshiba's 3-D Quantum denoising allows for reducing patient radiation exposure by up to 40% without loss of image quality. Each Toshiba Aquilion 64 CT scanner also features volume reconstruction, enabling to scan a large volume in a minimum of time as Volume Viewing automatically reconstructs scanned data into the isotropic volume used for diagnosis [11].

Preference was given to multislice computed tomography (MSCT) due to its simplicity and the ability to determine density during this investigation. Density calculations were based on the Hounsfield scale – a scale of gray shades widely used in MSCT. This scale is relative, with water (density assumed as 0 HU) and air (-1000 HU) as benchmark values. Each organ and tissue has its characteristic density value, and in the presence of pathological processes, radiological density may decrease (or more rarely increase). The obtained images were examined using the RadiANT DiCOM Viewer program [12].

All individuals included in the study were divided into two groups: the first group consisted of individuals with insulin resistance which was confirmed based on the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) study [13]. An essential condition for inclusion in the first group was the presence of prolonged elevation of HOMA-IR (for at least 2 years). HOMA-IR is calculated as the product of fasting insulin (μU/mL) × fasting glucose (mmol/L)/22.5.

To conduct the study, venous blood was drawn from individuals in the morning on an empty stomach, 8-12 hours before food intake for subsequent parameter calculation.

In the study group, HOMA-IR values ranged from 2.93 to 3.12. In the control group, they did not exceed 2.7.

Calculation of minimum and maximum density was performed by a medical expert in the area of the upper wall of the maxillary sinus, specifically the bony wall closest to the sinus cavity. Our interest in the maxillary sinus was primarily due to its frequent involvement in pathological processes compared to other paranasal sinuses. This could be explained by its larger size, proximity to teeth, and the natural opening located higher relative to its floor. The upper wall of the maxillary sinus may contain dehiscences and serve as a source for the spread of pathological processes to adjacent organs and tissues (orbit, cranial cavity).

Unfortunately, all our previous attempts to find anatomical landmarks for determining density that corresponded to its maximum and minimum values were unsuccessful. In this context we proposed using the uncertainty calculation for calculating radiological density. Uncertainty, as known, is a measure of measurement inaccuracy, showing the entire range of values reliably representing the investigated parameter. Interestingly, this method had previously been successfully used in laboratory diagnostics. We were the first to propose using the uncertainty calculation method to determine radiological density [14], successfully introducing this method into other medical fields [15].

The total standard measurement uncertainty of the thickness of the walls of the paranasal sinuses $U_c$ is calculated using the following formula:

$$U_c(H_H) = \sqrt{u_A^2(H_{Hi}) + u_B^2(H_{Hi})}\,, \tag{1}$$

where $u_A(H_{Hi})$ is the standard type A uncertainty, $u_B(H_{Hi})$ is the standard type B uncertainty.

The standard type A uncertainty is calculated using the following formula:

$$U_A(H_{Hi}) = \sqrt{\frac{1}{n(n-1)}\sum_{i=1}^{n}(H_{Hi} - H_H)^2}\,, \tag{2}$$

where $H_{нi}$ is the i-e value of sample measurement, $H_н$ is the mathematical expectation, n is the number of measurements in a sample.

Standard type B uncertainty is calculated using the following formula:

$$u(H_H) = H_H \frac{\delta_H}{\sqrt{3}\cdot 100}, \tag{3}$$

where $\delta_H$ is measurement error of the tool not exceeding 0.0001% [24,25]. The results of calculations of the total standard measurement uncertainty of the density (H) of the wall of the maxillary sinus are presented in Table 1. Then the interval estimate of uncertainty is performed, namely, the expanded uncertainty U according to the following formula:

$$U = ku_c\,, \tag{4}$$

where k is the coverage factor, which depends on the distribution law of the measured value and the chosen confidence level (p).

In this case, assuming a normal distribution, the coverage factor for a 95% confidence level is taken as 2.

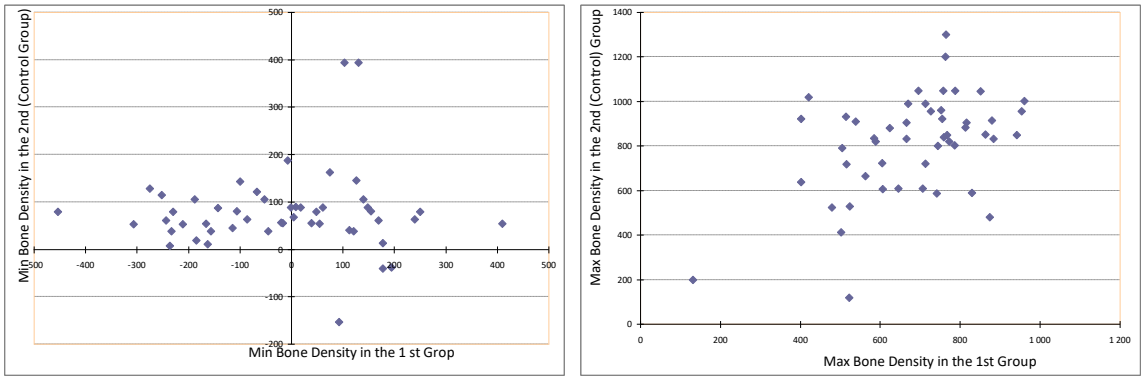
## 3. Results

The results of our study indicate a potential influence of insulin resistance on the bone density of the paranasal sinuses, specifically the upper wall of the maxillary sinus in our case. The minimum density was found in the group of individuals with insulin resistance. Particularly

noteworthy is the observation that both minimum and maximum bone density decreased in this group. The results are presented in Table 1.

**Table 1**
**The results of the study of bone density (HU - Hounsfield Units) in the maxillary sinus (1st and 2nd Groups)**

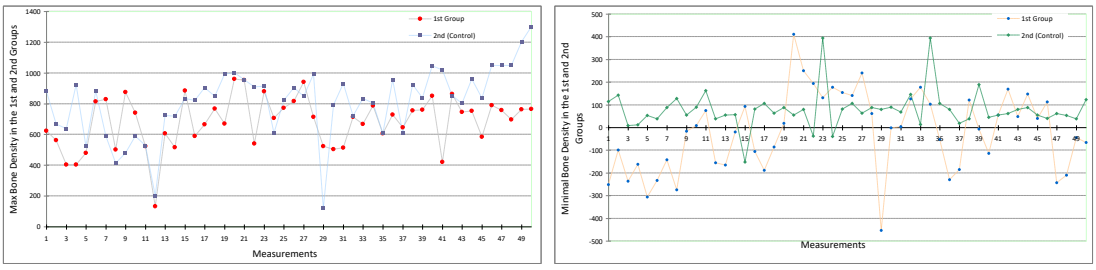
| Indicator | 1st Group Max | 1st Group min | 2nd Group Max | 2nd Group Min |
|---|---|---|---|---|
| UA(HHi) | 23.461 | 24.614 | 30.94 | 12.14 |
| UB(HHi) | 0,00039307 | -0,00001165 | 0.00046 | 0.00004 |
| Uc | 23.46 | 24.614 | 30.94 | 12.14 |
| U | 46.92 | 49.22 | 61.87 | 24.2885 |




a b

**Figure 1:** The specific values of minimum and maximum bone density in the investigated (Group 1) and control (Group 2) groups

As evident from Table 1 and Figure 1 a, b, density is unevenly distributed in both groups. In the investigated group, the minimum values fluctuate in the range of -470 HU to 250 HU, whereas in the control group, these values are noticeably higher, ranging from -150 HU to 400 HU (Figure 2 b). Maximum density values in the two groups show the same trend (Figure 2a). In the investigated group, the maximum density ranges from 170 HU to 990 HU, while in the control group, it is determined within the range of 130 HU to 1300 HU. For a better understanding of the density differences between the control and investigated groups, these values are graphically represented in Figure 2.




a b

**Figure 2:** The differences between the minimum and maximum density in both groups

The differences between the minimum and maximum density in both groups are as follows:
In the investigated group:
Minimum density: -470 HU to 250 HU
Maximum density: 225 HU to 1000 HU
In the control group:
Minimum density: -150 HU to 400 HU

Maximum density: 200 HU to 1300 HU

These ranges highlight the variability in bone density within each group. The minimum density represents the lower limit, while the maximum density represents the upper limit observed in each group. The differences in these ranges may indicate variations in bone density patterns between the investigated and control groups.

To identify a risk group, we calculated the difference between the minimum and maximum density in the two groups (fig. 3). Thus, it can be assumed that individuals with the highest difference values may constitute a risk group for the development of various pathological processes, including inflammatory processes in the paranasal sinuses and their complications.

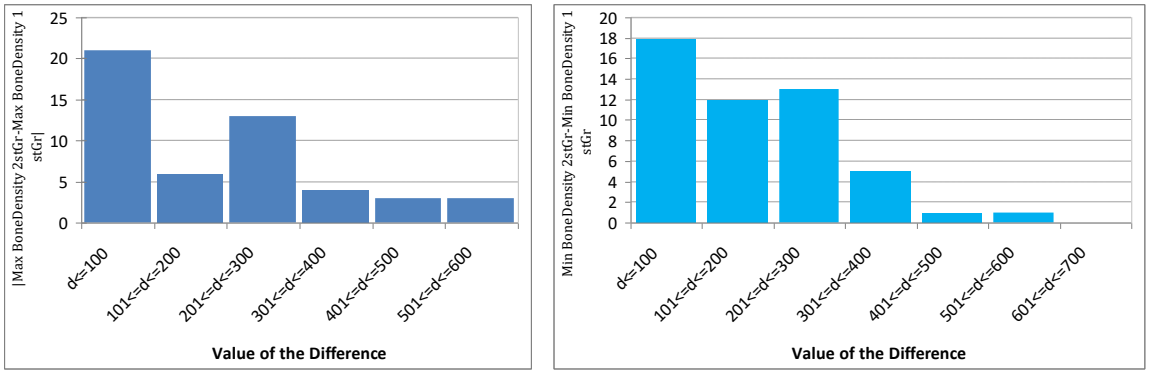



**Figure 3:** The difference in the values of maximum and minimum radiological density in the two groups

The difference in the values of maximum and minimum radiological density in the two groups is as follows:

In the investigated group: Difference=(Maximum Density)−(Minimum Density) = (1000HU)−(−470HU)=1470HU

In the control group Difference=(Maximum Density)−(Minimum Density) = (1300HU)−(−150HU)=1450HU

These values represent the range or spread of radiological density within each group. In this context, a higher difference may suggest a greater variability in bone density patterns within the group.

## 4. Discussion

Bone density, a critical indicator of bone tissue structure [16], holds immense importance for both long tubular bones, influencing outcomes such as the occurrence of hip fractures and associated complications in elderly individuals, as well as cancellous bone tissue [17]. The algorithms presented for tissue density calculation exhibit certain drawbacks, primarily linked to the specific selection of anatomical landmarks for density computation, which may not consistently reflect the actual values of this indicator.

The assessment of bone density, particularly in spongy bone tissue, is a highly intricate process that heavily relies on the specific coordinates chosen on the CT scan. Even minor variations in the examination point can significantly impact the accuracy of density measurements. Density is commonly expressed in relative units known as Hounsfield units [18, 19], with each type of tissue possessing a specific density value under normal conditions. It's noteworthy that there is a relatively limited number of worldwide studies dedicated to bone density, with most conducted on animals, likely due to the intricate nature of these measurements. Nevertheless, the importance of accurate density measurement should not be underestimated [20].

During the process of the analyzing obtained data, it is important to take into account information, which is related to the insulin and resistance to insulin

Research conducted in vitro has revealed that insulin exhibits a dual impact on bone metabolism. It diminishes the activity of osteoclasts by reducing the RANKL signaling pathway, thereby suppressing bone tissue degradation processes. Simultaneously, insulin stimulates osteoblasts, promoting osteogenesis and facilitating the formation of new bone tissue [21].

The work of Fulzele and colleagues [22] provides evidence that the insulin receptor plays an integral role in the proliferation, survival, and differentiation of osteoblasts. It also suppresses the inhibitor Runx2, a transcription factor that determines the differentiation of osteoblasts. These findings support the notion that insulin has a positive influence on bone tissue formation.

The authors also note that insulin stimulates the production of osteocalcin, the most prevalent protein specific to osteoblasts, which plays a crucial role in regulating bone formation processes [23]. It is important to highlight that there is a positive feedback loop, as osteocalcin, in turn, enhances insulin secretion and improves sensitivity to insulin.

In the future, it would be interesting to explore the density of skull bone tissue using new technologies, considering not only insulin resistance but also other accompanying conditions in order to implement it into the medical practice. The investigation of bone density involves a multidisciplinary approach, incorporating insights from various sources in the literature. Studies by Nazaryan et al. [24] and Popova et al. [25] delve into the oral health indices and the impact of electronic cigarettes on oral microbial flora, shedding light on potential factors influencing bone density. Furthermore, research by Denga et al. [26] explores the influence of metabolic syndrome on the microcirculatory bed of the oral cavity, offering valuable insights into systemic factors that may affect bone health.

The role of nitric oxide synthase in modulating the immune response in atopic diseases is explored by Nazaryan et al. [27], providing a deeper understanding of immune-related aspects affecting bone density. Fesenko et al. [28] investigate the consequences of microcirculatory disturbances in the oral mucosa, presenting a potential link between oral health and conditions such as rheumatoid arthritis.

In the context of technological advancements, the works of Izonin et al. [29], Yakovlev et al. [30], and Alekseeva et al. [31] highlight the application of smart technologies and intelligent decision support systems in the healthcare domain. These technologies may contribute to a more comprehensive assessment of bone density, potentially offering innovative approaches for evaluation.

Moreover, Gargin et al. [32] apply computer vision systems for the evaluation of pathomorphological images, demonstrating the integration of advanced imaging techniques in bone density assessment. The intelligent expert system by Chumachenko et al. [33] focuses on knowledge examination related to infections, showcasing the broader implications for systemic health, including bone density.

In the evolving landscape of healthcare, the exploration of smart systems and data-driven services by Izonin et al. [34] presents a broader perspective on how technology can be harnessed for holistic healthcare solutions, with potential implications for bone health.

As a result of this study, it was determined that, with the onset of insulin resistance, the minimum bone density tends to be significantly affected. This could serve as a prognostically unfavorable factor, as it is plausible to assume that the value of the minimum bone density may hold greater significance for the development of complications. It means patients who exhibit a notable difference in the minimum density compared to the control group deserve special attention, as this could potentially be associated with the occurrence of complications related to inflammatory processes within the paranasal sinuses in the future.

## 5. Conclusion

The study investigated the impact of insulin resistance on the density of the upper wall of the maxillary sinus. Through the use of the uncertainty calculation method, it was observed that insulin resistance tends to lead to a reduction in the minimum density of the upper wall of the maxillary sinus. This trend could serve as a trigger for the development of pronounced

inflammatory changes in the paranasal sinuses and act as a substrate for the onset of complications.

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