# Investigations into human tracheal cartilage osseocalcineus metaplasia
# III. ventro-dorsal measurement of the thickness of human tracheal cartilages

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The aim of the study was to verify the hypothesis that osseocalcineus metaplasia present in the tracheal cartilage is conditioned by its thickness. The study group comprised 78 male tracheas (age ranging between 19 and 84 years, mean = 56.5 years ±12.6 years), and 69 female tracheas (age ranging between 18 and 90 years, mean = 65.3 ±14 years). Tracheal transverse segments (every 4 cm) were collected for histopathological examinations from organs fixed in 10% formalin solution. Typical paraffin specimens, 5 μm thick, were measured in the horizontal position using the ocular micrometer (10 : 100 Zeiss) and Semiplan 3.2/0.10 objective. Differences between mean patient group and subgroup values were statistically verified. P = 0.05 was considered as statistically significant. Osseocalcineus metaplasia occurred 2.5-fold more often in male patients, in spite of the higher mean age of female patients ($p < 0.001$). The average male cartilage thickness was 50.32 ±7.94 × $10^{-2}$ cm, while that of female patients was 38.44 ±4.44 × $10^{-2}$ cm ($p < 0.001$). The average height of male patients (168.63 ±27.14 cm) was significantly higher in comparison to female patients (157.2 ±5.78 cm) ($p < 0.001$). The thickness of tracheal cartilages in men was significantly greater in metaplastic tracheas than in tracheas without metaplasia, as well as in changed cartilages as compared to unchanged ones in the same trachea. Considering both genders, the thickness of tracheal cartilages positively correlated with patient age (men: +0.44; $p < 0.001$; women: +0.293; $p < 0.014$), whereas height did not correlate with cartilage thickness.

**Key words:** tracheal cartilage, metaplasia, morphometry.

## Introduction

Osseocalcineus metaplasia of the tracheal cartilages develops with age, more often and earlier in the case of men as compared to female patients [1-3]. The pathomechanism of metaplasia development is unknown, although probably multifactorial. Tracheal cartilages do not possess vascularization. Nutrition is possible by means of diffusion of nutritional substances from the inferior thyroid artery, internal thoracic artery and thoracic aorta [4, 5]. The thicker the cartilage, the longer diffusion from the perichondrium to the inner layers of the cartilage. This favours the development of retrograde lesions with osseocalcineus metaplasia as the final stage. Male patients are characterized by a more compact structure. Thus, their cartilages are probably thicker in comparison to female patients of asthenic structure [2, 6]. However, there is a lack of precise data considering the thickness of changed and unchanged tracheal cartilages, both in male and female patients. We have decided to fill this gap.

## Material and methods

The study material comprised 78 male tracheas, patient age ranging between 19 and 84 years (mean age: 56.5 ±12.6 years), and 69 female tracheas,

patient age ranging between 18 and 90 years (mean age: 65.3 ±14 years) ($p < 0.001$) fixed in 10% formalin for a period of two weeks. Transverse segments were randomly chosen every 4 cm of the trachea for histopathological examinations. Paraffin blocks were prepared and sliced horizontally into 5 µm-thick sections, stained in haematoxylin and eosin. The thickness of the cartilages was measured with an ocular micrometer (10 : 100 Zeiss) built in the Jena Ax10 ocular, and Semiplan 3.2/0.10 objective built in the Ergaval microscope. The material comprised 577 cartilages, being subjected to 7679 measurements (13.3 measurements per cartilage), including measurements of thickness of the cartilages with six types of pathological changes, described in our previous paper [7].

The obtained results were correlated with the mean patient age and height. BMI values were not determined, due to the lack of significant contributing data to the anthropological type of the human body [1]. Finally, we compared the differences between appropriate groups and subgroups, being subjected to statistical verification ($\chi^2$ test and Student's t-test). $P = 0.05$ was considered as statistically significant.

## Results

Tables I-VII present the obtained results. Osseocalcineus metaplasia was diagnosed in 47.6% of the explored material, and 2.4-fold more often in men as compared to women (Table I). The extensiveness of changes in the tracheas was also more severe in men than in women (Table II).

Table III demonstrates that the average age of female patients was significantly higher in comparison to men ($p < 0.001$), while the average thickness of cartilages and female height were significantly lower than in men ($p < 0.001$). The thickness of male and female cartilages positively correlated with patient age (men: +0.44; $p < 0.001$, women: +0.293; $p < 0.014$) (Fig. 1). There was no correlation between cartilage thickness and body height in neither men nor women. Additionally, male patients were diagnosed with significant differences considering mean thickness of cartilages of metaplastic tracheas and normal tracheas ($p < 0.05$). In men, the average thickness of cartilages of metaplastic tracheas was 51.86 ±6.89 × $10^{-2}$ cm, while in the case of unchanged tracheas it was 47.41 ±8.98 × $10^{-2}$ cm, with no significant differences between mean age and patient height (Table IV). In the case of female patients such differences were not observed, although the mean thickness of metaplastic tracheas was minimally greater as compared to unchanged tracheas.

The comparison of the mean thickness of metaplastic cartilages between male and female patients, as well as that of normal cartilages, demonstrated a statistically significant difference. The mean thick-

**Table I.** The occurrence of osseocalcineus metaplasia in the 147 investigated tracheas, considering patient gender

| Sex | Changes present | Without changes | Total | % |
|---|---|---|---|---|
| | N | N | | |
| Men | 51 | 27 | 78 | 65.38 |
| Women | 19 | 50 | 69 | 27.54 |
| Total | 70 | 77 | 147 | 47.62 |

*N – number of tracheas*

**Table II.** The extent of metaplastic tracheal lesions, considering patient gender the 147 investigated tracheas, considering patient gender

| Sex | Changes present | Without changes | Total | % |
|---|---|---|---|---|
| | N1 | N1 | | |
| Men | 113 | 88 | 201 | 56.22 |
| (N = 51) Women (N = 19) | 32 | 44 | 76 | 42.10 |
| Total (N = 70) | 145 | 132 | 277 | 52.35 |

*N – number of tracheas; N1 – number of cartilages*

**Table III.** Thickness of tracheal cartilages, considering patient gender, age and height

| Feature | Men | | | | Women | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | N | Min | Max | $\bar{x}$ ± SD | N | Min | Max | $\bar{x}$ ± SD | |
| Age (years) | 78 | 19 | 84 | 56.46 ±12.55 | 69 | 18 | 90 | 65.32 ±13.97 | 0.001 |
| Cartilage thickness (× $10^{-2}$ cm) | 78 | 32.28 | 70.56 | 50.32 ±7.94 | 69 | 30.13 | 51.02 | 38.44 ±4.44 | 0.001 |
| Body height (cm) | 76 | 160 | 182 | 168.63 ±27.14 | 68 | 146 | 166 | 157.20 ±5.78 | 0.001 |

*N – number of patients, Min – minimal value, Max – maximal value, $\bar{x}$ ± SD – mean value plus minus standard deviation; p – significance level*

**Table IV.** Patient's age, height and thickness of cartilages in normal and metaplastic tracheas in men

| FEATURE | CHANGED TRACHEA | | | | UNCHANGED TRACHEA | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | N | MIN | MAX | $\bar{x} \pm SD$ | N | MIN | MAX | $\bar{x} \pm SD$ | |
| Age (years) | 51 | 26 | 84 | 58.76 ±12.09 | 27 | 19 | 84 | 52.11 ±19.40 | 0.1 |
| Cartilage thickness (× $10^{-2}$ cm) | 51 | 39.17 | 70.56 | 51.86 ±6.88 | 27 | 34.98 | 66.36 | 47.41 ±8.98 | 0.02 |
| Body height (cm) | 50 | 162 | 182 | 167.64 ±33.17 | 26 | 160 | 180 | 170.54 ±5.37 | 0.7 |

*N – number of patients, Min – minimal value, Max – maximal value, $\bar{x} \pm SD$ – mean value plus minus standard deviation; p – significance level*

**Table V.** Patient's age, height and thickness of cartilages in normal and metaplastic tracheas in women

| FEATURE | CHANGED TRACHEA | | | | UNCHANGED TRACHEA | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | N | MIN | MAX | $\bar{x} \pm SD$ | N | MIN | MAX | $\bar{x} \pm SD$ | |
| Age (years) | 19 | 42 | 82 | 64.68 ±12.63 | 50 | 18 | 90 | 65.60 ±14.30 | 0.9 |
| Cartilage thickness (× $10^{-2}$ cm) | 19 | 31.03 | 44.63 | 39.77 ±3.61 | 50 | 30.13 | 51.02 | 38.09 ±4.74 | 0.2 |
| Body height (cm) | 18 | 147 | 165 | 156.94 ±4.30 | 49 | 146 | 166 | 157.30 ±4.50 | 0.8 |

*N – number of patients, Min – minimal value, Max – maximal value, $\bar{x} \pm SD$ – mean value plus minus standard deviation; p – significance level*

**Table VI.** Thickness of changed and unchanged cartilages in the same trachea in both sexes

| SEX | THICKNESS OF CHANGED CARTILAGES (× $10^{-2}$ CM) | | | | THICKNESS OF UNCHANGED CARTILAGES (× $10^{-2}$ CM) | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | N | MIN | MAX | $\bar{x} \pm SD$ | N | MIN | MAX | $\bar{x} \pm SD$ | |
| Men | 113 | 40.00 | 84.47 | 53.73 ±8.31 | 88 | 40.54 | 65.97 | 46.56 ±9.53 | 0.001 |
| Women | 32 | 29.00 | 48.64 | 40.30 ±4.08 | 44 | 33.86 | 47.39 | 39.14 ±3.52 | 0.2 |

*N – number of patients, Min – minimal value, Max – maximal value, $\bar{x} \pm SD$ – mean value plus minus standard deviation; p – significance level*

**Table VII.** Ventro-dorsal thickness of the of the 6 types distinquished changes of tracheal cartilages, considering patient gender (× $10^{-2}$ cm)

| TYPE OF CHANGE | MEN | | | | WOMEN | | | | p |
|---|---|---|---|---|---|---|---|---|---|
| | N | CARTILAGE THICKNESS | | | N | CARTILAGE THICKNESS | | | |
| | | MIN | MAX | $\bar{x} \pm SD$ | | MIN | MAX | $\bar{x} \pm SD$ | |
| 1 | 6 | 33.24 | 56.28 | 43.07 ±7.04 | 9 | 25.07 | 43.38 | 33.77 ±4.84 | 0.02 |
| 2 | 41 | 39.00 | 75.56 | 53.66 ±10.34 | 8 | 27.79 | 52.17 | 41.39 ±1.44 | 0.01 |
| 3 | 124 | 28.00 | 70.00 | 45.20 ±8.27 | 210 | 18.00 | 55.70 | 37.84 ±6.21 | 0.001 |
| 4 | 36 | 36.93 | 68.93 | 49.95 ±7.77 | 27 | 28.00 | 52.08 | 39.71 ±5.69 | 0.001 |
| 5 | 28 | 37.12 | 71.56 | 51.76 ±7.85 | 11 | 25.00 | 42.95 | 39.60 ±5.69 | 0.001 |
| 6 | 60 | 34.70 | 82.44 | 56.14 ±10.79 | 10 | 37.56 | 52.17 | 42.68 ±4.37 | 0.001 |
| **Total** | 295 | 28.00 | 82.44 | 49.76 ±10.08 | 275 | 25.00 | 55.70 | 38.24 ±6.13 | 0.001 |

*N – number of cartilages, Min – minimal value, Max – maximal value, $\bar{x} \pm SD$ – mean value plus minus standard deviation, p – significance level*
*Types: 1 – normal cartilage, 2 – chondrolysis and asbestoid foci, 3 – eosinophilic staining of cartilage, chondrocytic desintegration and calcium dust, 4 – massive calcium deposits, 5 – coexistence of calcium deposits and osseous metaplasia foci, 6 – osseous metaplasia of the cartilage*

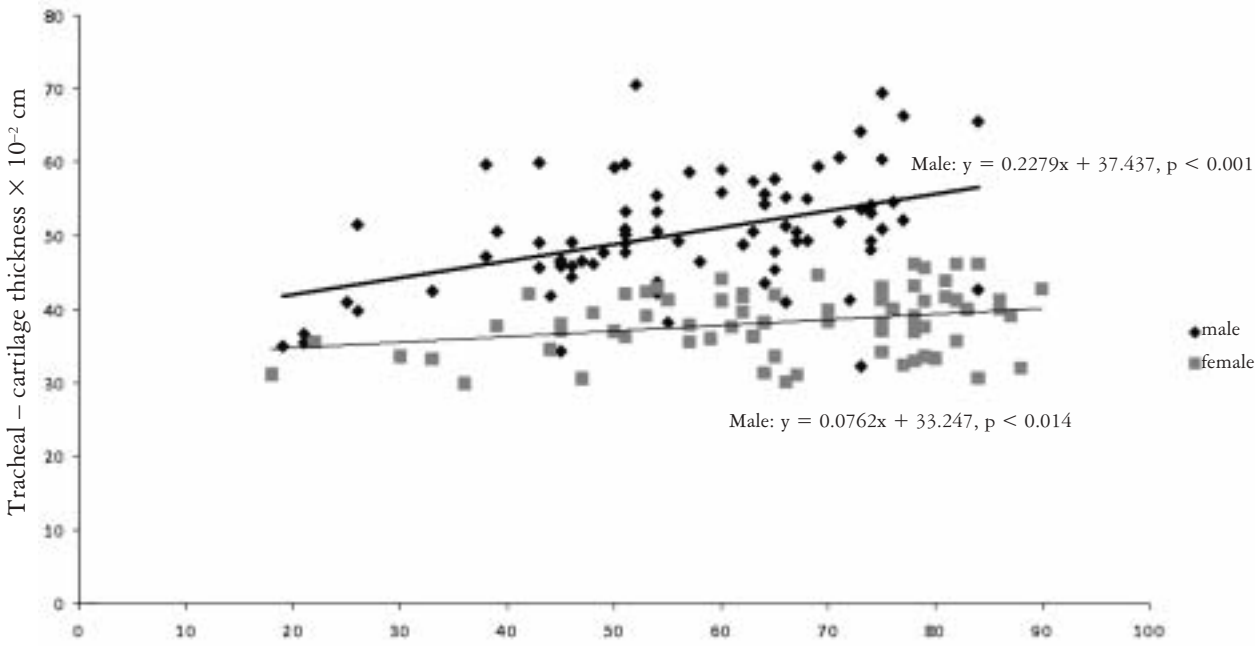


**Fig. 1.** Correlation diagram of age and tracheal cartilage thickness for male and female

ness of metaplastic and unchanged cartilages in the same trachea also showed a significant difference, but only in men (Table VI).

We also evaluated the relationship between the thickness of the cartilages, depending on the six diagnosed types of lesions (Table VII). The mean thickness of all male cartilage types was significantly greater than that of female patients. Considering both sexes, the healthy cartilages were significantly thinner than type 2, 4 and 6 cartilages. Type 2 (chondrolysis) and type 6 (osseous metaplasia) cartilages were the thickest. However, there were no statistically significant differences between these types.

## Discussion

The greater part of the cartilage is made up of extracellular matrix composed of water, type II collagen, and proteoglycans [8, 9]. With the process of aging the extracellular matrix is subjected to significant biochemical [1, 9, 10] and biomechanical changes [6, 11], which can be seen through increased hyalinization, granular-protein degeneration of chondrocytes, and ultrastructural swelling of colla – gen fibres with the deposition of calcareous salts on its surface [12]. We determined the final stage of the process, including asbestoid degeneration and ossification, as osseocalcineus metaplasia [3, 7].

Since this condition is diagnosed in 20-50% of the elderly, it is considered a physiological process connected with the process of aging [9]. In our material osseocalcineus metaplasia was observed in 47.60% of cases, nearly 2.5-fold more often in men as compared to women, already developing during the third decade of life [3, 9]. One should consider this a pathological process, being connected with the above-mentioned retrograde changes [1, 2, 9-12].

In our material the thickness of metaplastic and normal cartilages was significantly different in men, probably connected with the development of metaplasia. Such a connection was not observed in women. Here, the mean thickness of metaplastic and normal cartilages demonstrated no significant difference. Considering both sexes, the thickness of these cartilages was positively correlated with patient age. In spite of the fact that the average age of female patients was higher than that of men, the occurrence and extent of metaplastic lesions were significantly lower as compared to male patients. Osseocalcineus metaplasia in female patients occurred abruptly, although twenty years later than in men, that is during menopause, when the activity of gonads is decreased. One should consider that the oestrogens, which protect vessels, play an important role in the delayed atherosclerotic process, occurring later and with a dynamism of development much weaker than in men. In the end, the above factor could be responsible for the primary supply of nutritional substances to the tracheal cartilages. Unfortunately, no data are available in the literature. In our material, cartilage thickness measurements demonstrated that every above-mentioned type of change was significantly greater in male as compared to female patients. Thus, the following question arises: does the initial thickness of the cartilages condition the development of such lesions, or do they lead towards secondary

pathological distention of them? In both male and female patients the thickest cartilage was diagnosed when chondrolysis and osseous metaplasia foci developed. This question remains unresolved.

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