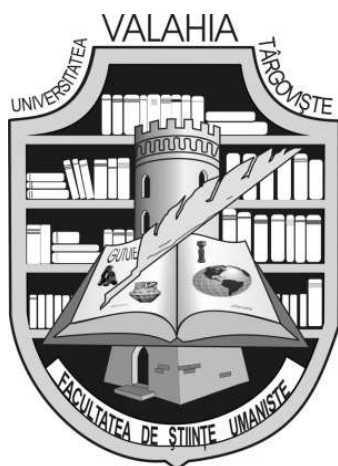


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A Case of Metastatic Carcinoma from XIIth – XIIIth Century Transylvania, Romania

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Abstract: The human skeletal remains analyzed in this study come from the medieval cemetery of Feldioara, Romania (XIIth – XIIIth centuries). A total number of 144 individuals were identified in the 124 graves excavated in several field periods between 1990 and 2007. In this work the characteristics of osteolytic lesions, identified in a skeleton of a 30–34 years old female, are discussed. All the skeletal elements available for analysis were subject to careful macroscopic and radiologic evaluations. Numerous lesions with various shapes and dimensions ranging between 2 mm and 25 mm were present in both cranial and post-cranial skeleton. All the characteristics of the pathological changes are indicative of a metastatic carcinoma. While a precise diagnosis of the primary lesion is not possible, the characteristics of the lesions as well as the age and sex of the individual suggest that the metastatic carcinoma originated from a breast cancer. Nevertheless, other types of tumors such as pulmonary cancer cannot be excluded.

Key words: Osteolytic skeletal lesions, metastatic carcinoma, Middle Ages, Feldioara, Transylvania.

Introduction

Metastatic bone cancer is the most common malignant tumor which affects the skeleton (R.E. Coleman, 1997; C.A. Roberts, K. Manchester, 2005). The skeletal metastases affect 85 % of the patients with soft tissue carcinomas (H.D. Dorfman, B. Czerniak, 1998) and certain types of soft tissue carcinomas – breast, prostate, lung and thyroid cancers – have a high tendency in producing bone metastasis.

In archaeological records the metastatic carcinoma are relatively rare, despite the fact that in the last twenty years the number of reported cases increased considerably. E. Strouhal (2001 in L.L. Capasso, 2005) noted that in the ancient Europe only 176 cases of malignant tumors were reported and estimated that approximately 43.2% of them are due to metastatic carcinoma. With some exceptions (e.g. E. Molnar *et al.*, 2009), most of neoplasms reporting are individual cases which are used in the recording of temporal and spatial distribution of various types of cancers in different human populations (S Webb, 1995).

The purpose of this paper is to describe the lesions identified on the skeletal remains of one individual from Feldioara collection that are compatible with a malignant tumor diagnosis and to suggest a possible diagnosis.

The cemetery

Feldioara is located on the left bank of the Olt River, 17 km north-west of Braşov. Two different names are known for Feldioara: “Földvár”, equivalent to the Romanian version “Feldioara”, which comes from Hungarian and means “earth fortress” and “Marienburg” (Saint Mary’s Fortress), name used by the German settlers which probably dates from 1211, when the Teutonic Knights were granted land in the Țara Bârsei. Based on the analogy given by the city Marienburg (Malbork) from northern Poland, which was founded in the middle of the XIIIth century, Feldioara is considered as the principal headquarters of the military-political administration exercised in Transylvania by the

Teutonic Knights between 1211 and 1225 (H. Zimmermann, 1996).

The Medieval cemetery was found between the evangelical church and the parsonage and it was partially excavated in several field campaigns between 1990 and 2007. The extremely poor funeral inventory, together with the presence of the grave niche for the head are the defining features of the Feldioara cemetery (A. Ioniță *et al.*, 2004). As grave goods, besides some Roman coins that do not help us in establishing the chronology, six anonymous Hungarian denars ascribed to Geza II (1141 – 1161) and Stephan III (1162 – 1172) were found, as well as three earrings with the end in “S” form, which place the cemetery in the second half of the XIIth century (A. Ioniță *et al.*, 2004). This suggests that the burials belonged to 2 – 3 generations from the last years of Geza’s II reign until the installation of the Teutonic Knights (1211).

Analogies with the cemeteries of Western Europe and with those from Transylvania, all located in the Saxon colonization area, show that the cemetery from Feldioara belonged to the first wave of German settlers who arrived in Transylvania after the middle of the XIIth century (A. Ioniță *et al.*, 2004).

The skeletal material

The skeletal remains found in the grave M.47 were fairly well preserved, with the exception of the skull which displayed extensive areas of surface erosions. Most of the skeletal elements were available for analysis (except the sternum and some of the hand and foot bones) but the ribs and the vertebrae were fragmentary. Age and sex were determined using standard techniques (R.S. Meidl, C.O. Lovejoy, 1989; J.E. Buikstra, D.H. Ubelaker, 1994). Based on the morphology of the auricular surface of the iliac bone (R.S. Meidl, C.O. Lovejoy, 1989), the age at death was assessed at 30 – 35 years. The skeleton was assessed as female, based on the morphology of the pelvic bones and skull.

Macroscopical and radiological findings

Several lytic and mixed lesions with variable dimensions were identified in the skull, vertebrae, sacral bone, left clavicle and scapula, innominate bones, humeri and femora (Fig.1). No pathological change was present in the lower limb bones distal to the femora and in the

forearm bones, with the exception of the right radius.

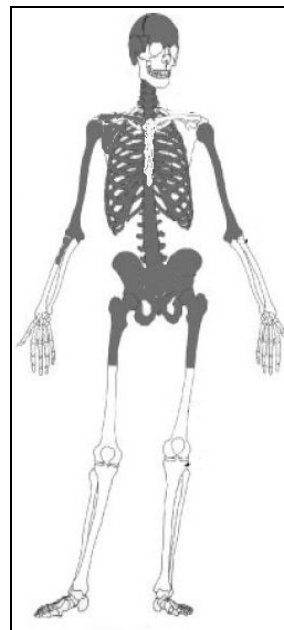


Figure 1- Distribution of the lesions in skeleton M.47.

The macroscopic evaluation of the skull revealed the presence of three lytic lesions. One circular lesion present on the left parietal bone, near the sagittal suture, penetrated both external and internal laminae of the bone and has a diameter of approximately 10 mm.

A second defect, with a diameter of 2 mm, is located in the right part of the frontal bone near the fronto – sphenoid suture and is penetrating only the external lamina of the bone. The cortical margins of this lesion presented small pitting. Finally, a third lesion with irregular contour destroyed completely the right occipital condyle. Several other lesions with variable sizes and cloudy contours were visible on the radiographs of the skull (Fig.2).

Several well-defined osteolytic focuses were visible on the cervical, thoracic and lumbar vertebrae, affecting both the vertebral bodies and the neural arches (Fig.3). Similar lesions were found also in the sacral bone. Their dimensions were highly variable and in some of the lesions deposits of new formed bone were identified. Eleven rib fragments showed multiple well – defined, rounded or ellipsoidal lytic focuses with variable dimensions. Their cortical margins presented small pitting and the interior of the

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lesions showed the presence of sclerotic bone. The radiograph of these fragments revealed the presence of several other smaller lesions that were not visible on the external part of the bones.

In the left clavicle, several lytic defects were identified close to the acromial end of the bone and a third one in the sternal end of the bone. The left scapula displayed a big lesion (maximal



Figure 2 - Lateral radiograph of the skull revealing multiple lytic lesions, not visible in the macroscopic examination.

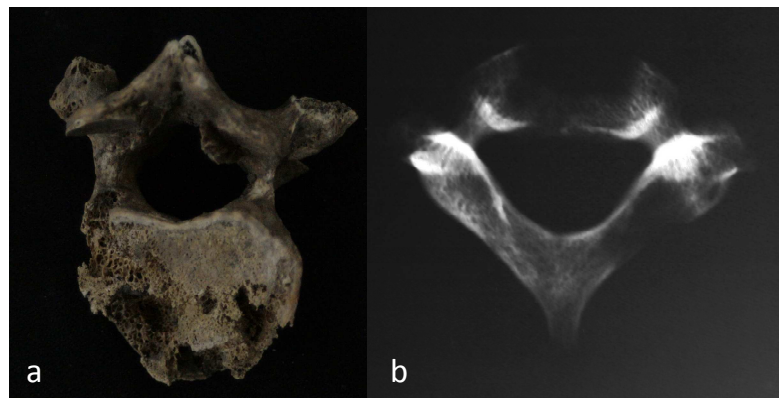


Figure 3 - Osteolytic lesions in vertebrae: (a) thoracic vertebra – inferior view, displaying multiple lesions with variable sizes in the vertebral body; (b) radiograph of a cervical vertebra (superior view) with lytic lesions in the vertebral body and the neural arch.

dimensions: 16 mm x 20 mm) with irregular shape, located inferior to the glenoid surface. Several other smaller lesions were visible on the

X-ray image (Fig.4 a). Remodeled and buttressing bone was present in the interior of the lesion (Fig.4 b).

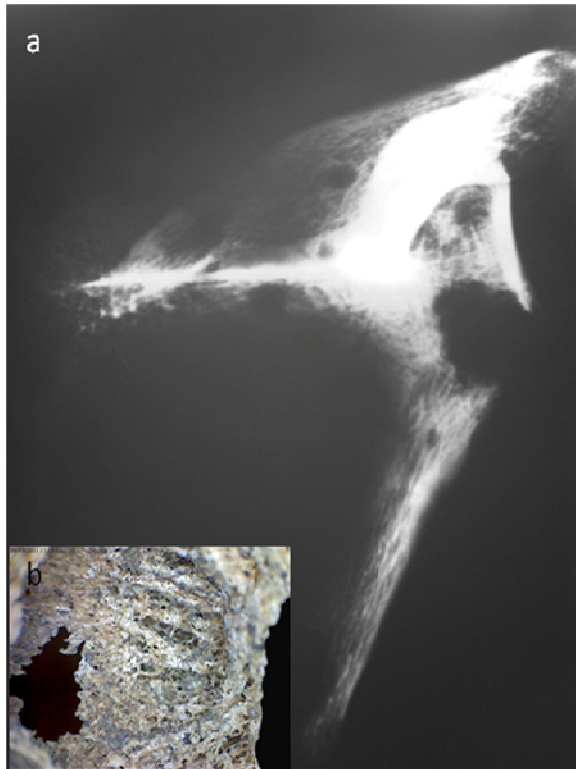


Figure 4 - Radiograph of the left scapula (a) showing multiple lytic destructions of the bone with variable shapes and dimensions; (b) detail of the lesion situated inferior to the glenoid surface showing the presence of buttressing bone.

In the upper limb skeleton, both humeri and right radius displayed multiple destructions in the proximal epiphysis and in the radial tuberosity respectively (Fig.5). The lesions with irregular shapes had dimensions varying between 4 mm and 16 mm in humeri and between 6 mm and 13 mm in radius.

Numerous osteolytic lesions were present also on the innominate bones (Fig.6). They are variable in shape, their dimensions vary between 2 mm and 25 mm and some of them coalesced. On the external surface of the right innominate bone, inferior to the wing of ilium, there is a relatively large area of sclerotic bone.

Similar lesions were identified also in the proximal ends of the femora. The right femur presented lesions in the femoral head and the neck of the femur, so much that the greater trochanter was completely destroyed (Fig.7). The proximal part of the left femur was fragmentary, but in the femoral head several lesions with remodeled surfaces (Fig.8) were identified.

Discussions

The lesions identified in the skeleton M.47 could be ascertained to either metastatic carcinoma or multiple myeloma. The differential diagnosis between the two conditions is often difficult because of the similarities between the bone lesions (D. Ortner, 2003; B.M. Rothschild *et al.*, 1998). However, several differences in terms of distribution, size and shape of the lesions exist between them.

Multiple myeloma is a highly malignant condition of the plasma cells and nowadays it represents almost 10% of all hematologic cancers (R.A. Kyle, S.V. Rajkumar, 2004). Usually it affects elderly individuals (only 3% of the affected individuals are younger than 40 years) and it is more common in males than in females (R. Hoffmann *et al.*, 2008). The most affected bones are the vertebrae, ribs, skull, hip bones, sternum, femur and humerus (D. Ortner, 2003; C.A. Roberts, K. Manchester, 2005). Multiple myeloma produces well defined osteolytic lesions with dimensions ranging between 0.5 mm and 20 mm (D. Ortner, 2003; B.M. Rothschild *et al.*, 1998). The lesions are generally spherical or rounded and give the impression of “punched out” areas (C.A. Roberts, K. Manchester, 2005). The osteoblastic reactions are inhibited by the plasma cells, therefore the presence of sclerotic margins is very unlikely (D. Brothwell, 2008; D. Ortner, 2003).

Metastatic carcinomas arise from primary tumors of the epithelial tissues. The malignant cells disseminate from the primary tumor through bloodstream or lymphatic system and produce secondary neoplasms (R.E. Coleman, 1997; D. Ortner, 2003). It occurs relatively late in life and is more frequent in females than in males (H.D. Dorfman, B. Czerniak, 1998). The skeletal system is the third preferred site for metastasis development, after the lungs and liver (R.E. Coleman, 1997). In the skeleton, metastatic carcinoma can produce osteolytic, osteoblastic or mixed lesions (D. Ortner, 2003; C.A. Roberts, K. Manchester, 2005). While the presence of osteoblastic and mixed pathological changes is clear indicative of metastatic carcinoma, the differential diagnosis between osteolytic metastatic carcinoma and multiple myeloma is more difficult. Generally, osteolytic metastatic carcinomas lesions are variable in size (D. Ortner, 2003) and have elliptical or geogra-

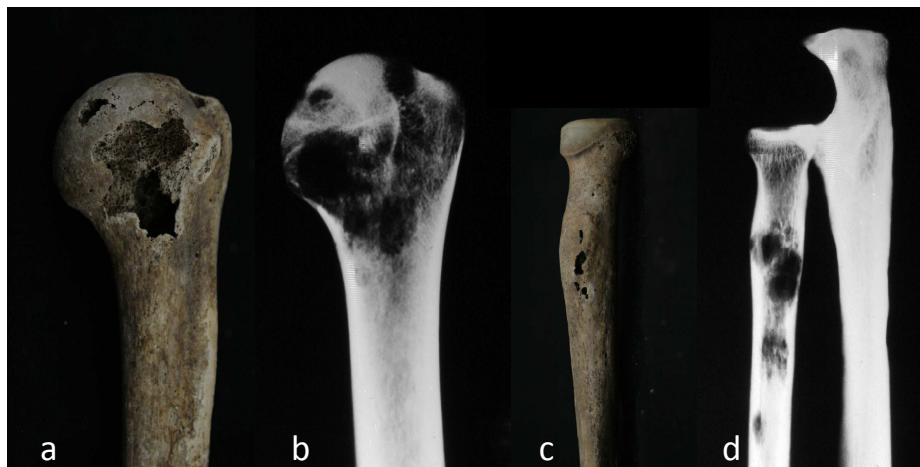


Figure 5- Well defined osteolytic lesions in the proximal end of the left humerus (a – b) and in the proximal third of the right radius (c – d). The right cubitus do not display any lytic lesions (d).

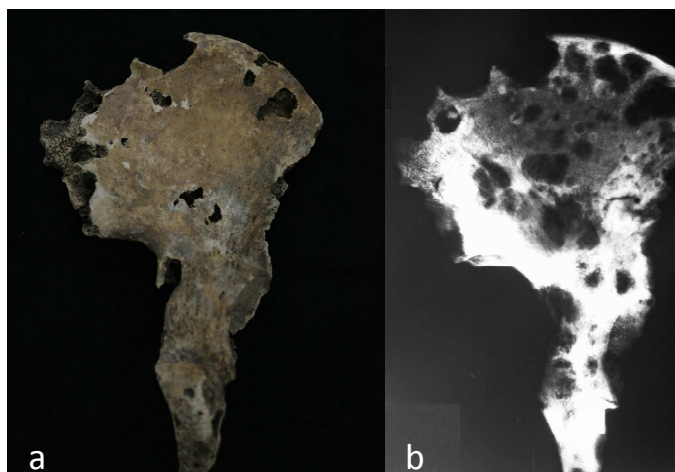
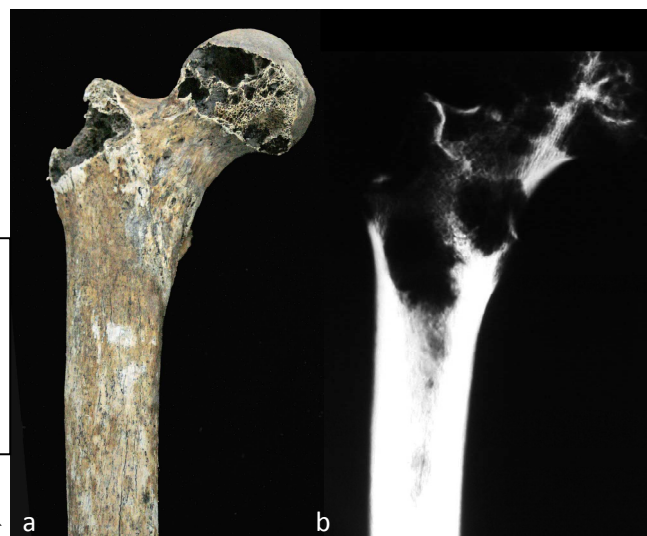


Figure 6 - External surface of the right innominate bone (a) and radiograph (b) revealing the presence of numerous well defined osteolytic lesions.

Figure 7. Anterior view of the proximal third of the right femur (a) and radiograph showing the presence of multiple lytic destructions (b).



phic shape (B.M. Rothchild *et al.*, 1998). In the same time, the osteolytic lesions produced by metastatic carcinoma show a non-malignant new bone formation and the presence of buttressing and sclerotic bone, which is uncommon in multiple myeloma (M.K. Marks, M.D. Hamilton, 2007; D. Ortner, 2003; B.M. Rothchild *et al.*, 1998). Like multiple myeloma, metastatic carcinoma affects frequently the axial skeleton, the hip bones and the proximal portions of the

femur and humerus (D. Ortner, 2003). The involvement of the bones located distal to the elbow or to the knee is rare in metastatic carcinoma (M.K. Marks, M.D. Hamilton, 2007; D. Ortner, 2003). The review of the clinical literature showed that only 7% of the bone metastasis cases involve the skeletal elements situated below the elbow or the knee (S. Kundu *et al.*, 2007).

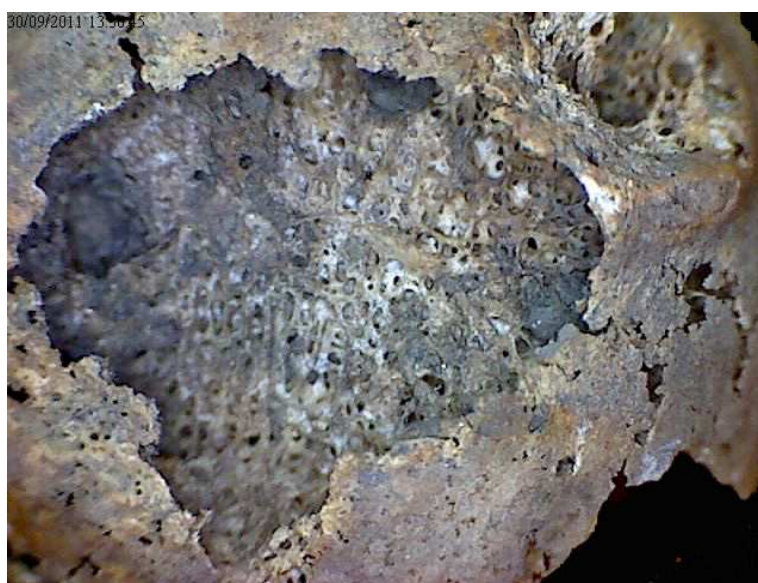


Figure 8. Detail of a mixed irregular shaped lesion in the head of the left femur with remodeled surface.

The adult female identified in the grave M.47 exhibits multiple osteolytic lesions with characteristics compatible with the diagnosis of metastatic carcinoma. These lesions that have variable sizes and irregular shapes, are more common to metastatic carcinoma than to multiple myeloma. In the same time, the skeletal distribution of the lesions, involving both the cranial and the post-cranial skeleton, are typical for both conditions. More surprising is the involvement of radius which is rare in metastatic carcinoma and more common in multiple myeloma (M.K. Marks, M.D. Hamilton, 2007; D. Ortner, 2003). However, the extensive presence in several foci of an osteoblastic response as well as the sclerotic character of some of the lesion makes multiple myeloma an unlikely diagnosis for this case.

In archaeological skeletal remains, the identification of the primary cancer site is often impossible. Nevertheless, the clinical data show that several carcinomas (Tab. 1) have a high tendency in generating bone metastasis (D. Ortner, 2003; M.K. Marks, M.D. Hamilton, 2007).

Primary tumor	Incidence of bone metastasis
Breast	65 – 75 %
Prostate	65 – 75 %
Lung	30 – 40 %
Kidney	20 – 25 %
Thyroid	60 %

Table 1 - Incidence of bone metastases (after Coleman, 1997).

In women, the breast cancer is the most common type of primary carcinoma producing bone metastasis (R.E. Coleman, 1997) and generally the lesions are osteolytic (D. Ortner, 2003; M.K. Marks, M.D. Hamilton, 2007). The age, sex and the morphological and radiological characteristics of the osteolytic lesions identified in the skeletal remains of the individual M.47 suggest breast cancer as a probable site for the primary tumor, but other types of cancers (e.g. lung cancer, intestinal tract cancer) cannot be excluded. Breast cancer is the most frequent site of origin of bone metastasis in women and in the same time the life expectancy of affected persons is longer than in other types of carcinomas (e.g. lung cancer), which implies also a longer time to develop bone metastasis.

Conclusion

A case of metastatic carcinoma affecting an adult female (M.47) from Feldioara skeletal collection is reported. The morphological and radiological characteristics of the osteolytic lesions identified in the cranial and postcranial skeleton are compatible with this diagnosis. Moreover, in the differential diagnosis between metastatic carcinoma and multiple myeloma, the presence of sclerotic lesion makes the latter a less likely diagnosis for this case. The age and sex of the individual, as well as the patterns of the lesions suggest breast cancer as the primary tumor, but other types of carcinomas, such as lung cancer, cannot be excluded.

Metastatic carcinomas and cancers in general are rarely found in archaeological skeletal material and therefore their interpretation is made in terms of temporal and spatial distribution of different types of neoplastic diseases in past human population (E. Strouhal, 2001 in L.L. Capasso, 2005). Therefore it is important to reports all new cases of cancers, as this can contribute to our comprehension of these pathologies in the past. To our knowledge, the present case is the first reported case of metastatic carcinoma in Romania.

BIBLIOGRAPHY

Brothwell D., 2008, *Tumours and tumour-like processes*, in: R. Pinhasi, S. Mays, *Advances in human palaeopathology*, John Wiley & Sons, West Sussex, 408 p., ISBN 978-0-470-03602-0, p. 253–281.

Buikstra J. E., Ubelaker D.H., 1994, *Standards for Data Collection from Human Skeletal Remains*. Arkansas Archeological Survey Research Series No. 44, Fayetteville, 206 p., ISBN 1-56349-075-7.

Capasso L. L., 2005, *Antiquity of Cancer*, International Journal of Cancer, Volume 113, Issue 1, p. 2-13.

Coleman R. E., 1997, *Skeletal Complications of Malignancy*, Cancer Supplement, Volume 80, Number 8, p. 1588-1594.

Dorfman H. D., Czerniak B., 1998, *Bone Tumors*, Mosby, St. Louis, 1261 p., ISBN 0-815-12746-4.

Hoffman R., Furie B., Benz E.J. Jr., McGlave P., Silberstein L. E., Shattil S.J. (eds.), 2008, *Hematology: Basic Principles and Practice*, 5th Edition, Churchill Livingstone, Philadelphia, 2640 p., ISBN 978-0-443-06715-0.

Ioniță A., Căpățână D., Boroffka N., Boroffka R., Popescu A., 2004, *Feldioara / Marienburg Contribuții arheologice la istoria Țării Bârsei / Archäologische Beiträge zur Geschichte des Burzenlandes*, Editura Academiei Romane, Bucharest, 250 p., ISBN 973-27-1003-9.

Kundu S., Shankar S., Mitra S., Accharya S., Roy A., Dastidar A.G., 2007, *Below-Elbow and Below-Knee Metastases in Breast Cancer – A Case Report*, Indian Journal of Medical & Pediatric Oncology, Volume 28, Issue 3, p. 38-40.

Kyle R. A., Rajkumar S.V., 2004, *Multiple meloma*. The New England Journal of Medicine, No. 351, p. 1860-1873.

Marks M.K., Hamilton M.D., 2007, *Metastatic Carcinoma: Paleopathology and Differential Diagnosis*. International Journal of Osteoarchaeology, Volume 17, Issue 3, p. 217-234.

Meidl R. S., Lovejoy C.O., 1989, *Age Changes in the Pelvis: Implications for Paleodemography*, in M.Y. Iscan, *Age Markers in the Human Skeleton*, Charles C Thomas Pub Ltd., Springfield, 359 p., ISBN 0-398-05614-5, p. 137-168.

Molnár E., Marcsik A., Bereczki Z., Schmidt-Schultz T.H., Schultz M., Pálfi G. 2009. *Malignant tumors in osteoarchaeological samples from Hungary*. Acta Biologica Szegediensis, Volume 53(2), p. 117-124.

Ortner D. J., 2003, *Identification of Pathological Conditions in Human Skeletal*

Remains, Second Edition, Academic Press, Amsterdam, 645 p., ISBN 0-12-528628-7.

Roberts C. A., Manchester K., 2005, *The archaeology of disease*, 3rd Edition, Sutton

Publishing Limited, Stroud, 338 p., ISBN 0-7509-2683-X.

Rothschild B. M., HersHKovitz I., Dutour O., 1998, *Clues Potentially Distiguishing Lytic Lesions of Multiple Myeloma from Those of Metastatic Carcinoma*, American Journal of Physical Anthropology Volume 105, Issue 2, p. 241-250.

Strouhal E., 2001, *Malignant tumours in past populations in Middle Europe*. In: M. La Verghetta, L. Capasso, *Proceedings of the*

XIIIth European Meeting of the Paleopathology Association, Chieti, Italy, 2000, Edigrafical S. p. A., Teramo, p. 265–272.

Webb S., 1995, *Palaeopathology of Aboriginal Australians: Health and Disease across a Hunter-Gatherer Continent*, Cambridge University Press, Cambridge, 336 p., ISBN 978-0-521-46044-6.

Zimmermann H., 1996. *Siebenbürgen und seine Hospites Theutonici. Vorträge und Forschungen zur Südostdeutschen Geschichte, Festgabe zum 70. Geburtstag. In Auftrag des Arbeitskreises für Siebenbürgische Landeskunde herausgegeben von K. Gündisch*, Köln / Weimar / Wien, 357 p., ISBN 3-412-12795-7.