The Effects of Cancer Treatment-Induced Bone Loss on Morphological Sex Assessment

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Introduction

According to the American Cancer Society (2017), approximately 1,688,780 individuals will be diagnosed with cancer this year. Throughout the 20th and 21st centuries, cancer rates have steadily risen in the U.S. Increased cancer rates have also led to a rise in the development of new treatments. Many of the regimens used to treat and cure cancer affect normal bone metabolism by increasing osteoclastic activity and decreasing osteoblastic activity, resulting in a net loss of bone (Michaud and Goodin 2006). As such, one of the most pervasive side effects of cancer treatments is cancer treatment-induced bone loss (CTIBL).

The creation of an accurate biological profile (sex, age, ancestry and stature of skeletonized remains) is a vital component of any forensic anthropological analysis. Sex is especially important as it can be used to quickly limit the list of possible decedents, and sex dictates the methods used in age, ancestry, and stature estimations. Morphological methods are often used to assess sex, and these methods rely on examining the relative size and shape of sexually dimorphic traits, particularly of the pelvis and skull. However, CTIBL is known to affect both cortical and cancellous bone, in addition to creating a fertile niche within bone for cancer metastases (Figure 1). Therefore, if CTIBL affects cortical and trabecular bone, then the robusticity of the sexually dimorphic traits analyzed using morphological methods may decrease, and the overall sex assessment will skew towards gracile.

Figure 1. Metastasized cancer to cranium (UTK 62-11).

Materials and Methods

The sample consists of **330 individuals** (**f = 169, m = 161**) from the William M. Bass Donated Skeletal Collection at the University of Tennessee, Knoxville. A total of **169 individuals served as a control sample** with no known histories of cancer, while **161 individuals served as an experimental group** with documented histories of cancer. The experimental sample was further divided into a drug-based treatment subgroup and a surgery-based treatment subgroup. The cranial traits (nuchal crest, mastoid process, supraorbital margin, glabella and mental eminence) and the pelvic traits (ventral arc, ischiopubic ramus ridge, subpubic contour and greater sciatic notch) were scored using the methods outlined in Buikstra and Ubelaker (1994), Walker (2008, 2005), and Klales et al. (2012). Chi-square and ANOVA analyses were conducted to assess the relationship between cancer treatment status and the scoring of the traits; ANCOVA analyses were performed to assess the effects of age on the trait scores; and Cohen's kappa analyses were conducted to assess intraobserver agreement.

Results

Table 1. Results of chi-square analyses for sexually dimorphic traits and study subgroups (p-values).

Sexually Dimorphic Traits	Pooled-No sex (n=330)	Pooled-Female (n=169)	Pooled-Male (n=161)	Drug-No sex (n=201)	Drug-Female (n=95)	Drug-Male (n=106)	Surgery-No sex (n=129)	Surgery-Female (n=74)	Surgery-Male (n=55)
Ventral Arc	0.997	0.832	0.963	0.911	0.338	0.849	0.742	0.329	0.386
Subpubic Contour	0.800	0.273	0.983	0.791	0.645	0.856	0.532	0.104	0.399
Ischiopubic Ramus Ridge	0.965	0.810	0.367	0.466	0.907	0.184	0.654	0.722	0.187
Greater Sciatic Notch	0.435	0.897	0.422	0.428	0.429	0.617	0.215	0.191	0.464
Nuchal Crest	0.651	0.722	0.124	0.794	0.539	0.516	0.392	0.745	0.068
Mastoid Process	0.882	0.857	0.888	0.964	0.819	0.997	0.726	0.896	0.375
Supraorbital Margin	0.407	0.395	0.629	0.795	0.183	0.930	0.452	0.581	0.480
Glabella	0.596	0.047	0.607	0.794	0.361	0.485	0.748	0.173	0.655
Mental Eminence	0.227	0.106	0.964	0.480	0.424	0.721	0.110	0.146	0.647

Table 2: Results of ANOVA analyses for sexually dimorphic traits and study subgroups (p-values).

Sexually Dimorphic Traits	Pooled-Cancer (n=330)	Pooled-Sex and Cancer (n=330)	Drug-Cancer (n=201)	Drug-Sex and Cancer (n=201)	Surgery-Cancer (n=129)	Surgery-Sex and Cancer (n=129)
Ventral Arc	0.972	0.642	0.073	0.930	0.010	0.882
Subpubic Contour	0.707	0.282	0.422	0.359	0.100	0.785
Ischiopubic Ramus Ridge	0.567	0.851	0.236	0.595	0.541	0.599
Greater Sciatic Notch	0.898	0.528	0.681	0.771	0.594	0.203
Nuchal Crest	0.562	0.297	0.513	0.491	0.062	0.271
Mastoid Process	0.556	0.946	0.893	0.967	0.423	0.945
Supraorbital Margin	0.751	0.755	0.965	0.928	0.680	0.741
Glabella	0.099	0.222	0.251	0.639	0.292	0.208
Mental Eminence	0.503	0.876	0.643	0.963	0.630	0.864

Table 3: Results of ANCOVA analyses for age, sexually dimorphic traits and study subgroups (p-values).

Sexually Dimorphic Traits	Pooled (n=330)	Drug Subgroup (n=201)	Surgery Subgroup (n=129)
Ventral Arc	0.107	0.387	0.172
Subpubic Contour	0.018	0.148	0.086
Ischiopubic Ramus Ridge	0.001	0.005	0.051
Greater Sciatic Notch	0.095	0.078	0.663
Nuchal Crest	0.043	0.080	0.330
Mastoid Process	0.004	0.016	0.188
Supraorbital Margin	0.387	0.991	0.162
Glabella	0.898	0.676	0.413
Mental Eminence	0.886	0.938	0.863

Results, contd.

Table 4. Intraobserver agreement results.

Sexually Dimorphic Traits	Cohen's Kappa (k)	Level of Agreement (Landis and Koch 1977)
Ventral Arc	0.607	Moderate
Subpubic Contour	0.607	Moderate
Ischiopubic Ramus Ridge	0.587	Moderate
Greater Sciatic Notch	0.715	Substantial
Nuchal Crest	0.699	Substantial
Mastoid Process	0.636	Substantial
Supraorbital Margin	0.406	Fair
Glabella	0.720	Substantial
Mental Eminence	0.432	Moderate

Discussion and Conclusions

While the results indicate that cancer treatment does not affect the scoring of sexually dimorphic traits, age was found to affect several of the traits in the pooled group and the drug-based treatment subgroup. However, even when sex and age were controlled for, cancer treatment status was only slightly statistically significant for the ventral arc of individuals in the surgery-based treatment subgroup. Further, age was not a statistically significant variable for any trait including the ventral arc in the surgery-based treatment subgroup. Therefore, age did not mask the effects of cancer treatment status.

Cancer treatment status was statistically significant for the glabella of females in the pooled sample. Therefore, CTIBL may reduce the robusticity of this trait in females. Cancer treatment status was also statistically significant (e.g., reduced) for the ventral arc of females and males in the surgery-based treatment subgroup when sex was not considered as a variable. Therefore, in individuals who have undergone cancer treatment, it is advisable to use the ventral arc with caution. However, it is difficult to diagnose someone with CTIBL, which may present as osteoporosis; though, this is also a normal age-related pathology. The presence of lytic lesions caused by metastasized cancer may also be an indicator, but this is not definitive proof that someone has undergone cancer treatment. Overall, cancer treatment does not appear to affect the robusticity of sexually dimorphic traits, and therefore, the overall assessment of sex is not skewed towards gracile.

Unfortunately, there are several limitations to this study, such as a lack of antemortem data on the length of cancer treatment and timing of cancer treatment for each individual. Further, the sample was predominantly comprised of older European Americans; thus, the results of this study are not applicable to younger individuals or individuals from different ancestries. For example, African Americans generally display greater bone mineral density compared to European Americans (Walker and Bilezikian 2008), and this may impact the bony response to cancer and cancer treatment. Future research should incorporate clinical, MRI/CT data on those individuals with documented cancer treatment and duration. Other components of the biological profile, especially age, should be included, as well as incorporating other medications that are suspected or known to affect the skeleton.

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