MAGNETIC RESONANCE IMAGING OF CALVARIAL DIPLOE THICKNESS FOR SEX AND AGE ESTIMATION OF A SAMPLE OF EGYPTIAN POPULATION

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ABSTRACT

Background: Magnetic resonance imaging (MRI) is a mainstay radiological technique that is becoming more desirable in forensic identification for its non-invasive, non-ionizing and highly precise nature. **Objectives:** This study aimed to investigate whether sex and age could be estimated based on Calvarial Diploe Thickness (CDT) using MRI in a sample of the Egyptian population. **Methods:** The study was conducted on cranial MRI images of 306 adult Egyptians. For sex and age estimation, seven CDT measurements were assessed on 256 cranial MRI images of known sex and age. A binary logistic regression equation was developed for sex prediction. Multivariate linear regression analyses were performed to generate age prediction equations; equation (1), gender was included, while equation (2) was irrespective of gender. All regression equations were tested on 50 cranial MRI images. **Results:** The results revealed a significant binary logistical regression model for sex prediction of r^2 0.442 and classification accuracy 71.6%. The Receiver Operating Characteristic (ROC) curve showed an area under the curve (AUC) 0.816, sensitivity 76.6 %, and specificity of 70.5%. Testing the equation showed accuracy for identifying males (78.2 %), accuracy for identifying females (70.4 %), and overall accuracy (74 %). Regarding age estimation, Pearson correlation showed no statistically significant correlation between age and all CDT measurements. Age prediction multivariate linear regression models (sex-stratified/sex-pooled) were statistically insignificant, with very low adjusted r^2 and high standard error of estimate. Testing the multivariate linear regression equations showed Mean Absolute deviation (MAD) between the chronological age and predicted age of 9.09254 years and Mean Absolute Percentage Error (MAPE) of 28.458% for the multivariate linear regression equation (1) and MAD of 8.94469 years; and MAPE of 27.9829% for the multivariate linear regression equation (2). **Conclusion:** We concluded that the studied CDT measurements could be included as a new candidate in MRI-based sex estimation for Egyptians while are unfavorable for estimating age. Our results provide preliminary results for assessing a new approach for estimating sex and age for Egyptians. Applying such parameters on a greater sector of Egyptians for both sex and age estimation is highly recommended.

Keywords: Calvarial diploe thickness; age estimation; sex estimation; Magnetic Resonance Imaging; Egyptians

INTRODUCTION

"Virtual Anthropology" integrates various radiological modalities with anthropological characters to reach the forensic biological profile of both the living and dead. One of the most significant advantages of the virtual method is documenting and archiving virtual physical evidence throughout time **(Mallett et al., 2014; Guglielmi et al., 2015).**

Magnetic resonance imaging (MRI) is a transmissive radiological modality that functions by penetrating subjects to collect information about their volume; thus, avoiding maceration of bodies in the forensic context. Despite the substantial advancement of MRI, its medicolegal utilization has lagged far behind such enormous progress. MRI is advantageous in many aspects; it provides precision, sensitivity, and excellent multiplanar spatial resolution. Moreover, MRI is getting more desirable in the forensic age estimation of the living because of its non-ionizing nature, which confers an ethical justification for imaging the living **(Higginbotham-Jones and Ward, 2014; Franklin et al., 2016; Grabherr et al., 2016; Clemente et al., 2017; Neumayer et al., 2018; Carew and Errickson, 2019).**

From the forensic point of view, reaching the personal identity of an individual shall pass first by the station of estimating the biological profile, namely sex, age, ancestry, and stature. This narrows the pool of searching for the individuality of each victim. Doing so requires the anthropometric standards to be population-based and geographically specific if accuracy is required **(Franklin et al., 2016; Yasar Teke et al., 2018).** Accurate sex estimation narrows this search by half. Accordingly, establishing a human's biological profile and hence his identity usually starts with estimating sex **(Spradley, 2016; Kalim and Tyagi, 2018; Yasar Teke et al., 2018).** Another parameter of the biological profile to be assessed is age.

Regarding living, age estimation is demanded for both clinical and legal purposes. More studies are required in this aspect to validate the existing scoring systems by applying other non-ionizing modalities (e.g., MRI) and using various anatomical sites **(Aalders et al., 2017; Neumayer et al., 2018).**

The skull is a substantial element in forensic anthropology. It is one of the most extensively studied bony structures due to its excellent conservation nature. The skull morphological aspects have long been utilized for estimating both sex and age. However, metric-based research has always been objective, reliable, reproducible, and inferential **(Fortes de Oliveira et al., 2012; Santos et al., 2014; De Boer et al., 2016).** Anatomically the skull is a flat diploic bone, consisting of outer and inner plates of cortical bone and a layer of trabecular bone in between called "diploe". The extent to which measurement of diploe thickness of the cranial vault "calvarium" (Calvarial Diploe Thickness; CDT) can be used for estimation of age and sex is still under investigation **(Hatipoglu et al., 2008; Al-Khatieeb, 2011; Sabancıoğulları et al., 2012).** Moreover, the CDT studies will benefit researchers and scientists in multiple disciplines as anatomy, anthropology, and neurosurgery. The clinical benefit of such studies can guide calvarial bone grafting and skull fixation neurosurgeries **(Farzana et al., 2018).**

Accordingly, we aimed at investigating whether sex and age could be estimated based on CDT using MRI in a sample of the Egyptian population.

MATERIAL AND METHODS

The study was conducted on archived anonymized cranial MRI images of 306 adult Egyptian patients referred to the MRI unit at the Diagnostic Radiology Department of an Egyptian hospital to perform a clinical cranial MRI exam. Exclusion criteria included any cranial bone disorder, whether traumatic or pathological. MRI was conducted on a 1.5-T closed whole-body MR System (Achieva, Philips, Netherland). The maximum gradient capacity was 33 mT/m. Cranial MRI routinely includes sagittal and axial T1, axial and coronal T2, and axial FLAIR sequences. Table 1 shows the parameters of the MRI protocol.

Table (1): Parameters of MRI protocol

	TR	TE	Section thickness	Interval	Field of view	Matrix	NEX
T1-WI	400 ms	8.9 ms	5 mm	1.25 mm	24 mm_18 mm	288_256	2
T2-WI	4440 ms	101 ms	5 mm	1.25 mm	24 mm_18 mm	352_224	1
FLAIR-WI	8402 ms	102 ms	5 mm	1.25 mm	24 mm_24 mm	288_160	1

WI: Weighted Images
TR: Repetition time
TE: Echo time

MRI image analysis

After determining the following landmarks; Nasion is positioned at the frontonasal and internasal sutures meeting point, Bregma is positioned at the coronal and sagittal sutures intersection point, Lambda is positioned at the sagittal and lambdoid sutures meeting point, Opisthocranion is the most prominent posterior point on the occiput, Euryon is the most prominent lateral points on parietal bones, the seven CDT measurements were assessed on the sagittal and axial T1-WI (T1-Weighted Images) **(Sabancıoğulları et al., 2012).** On the dedicated MRI workstation, maximum magnification of the image was applied, reaching maximum zooming (500 %). Then, dimensions of CDT were measured (in millimeters; mm) between the deep surfaces of both inner and outer cranial tables (seen as low T1 signal lines) that were not included in the measurement.

Seven CDT were **(Sabancıoğulları et al., 2012):**

On Midsagittal T1

CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) **(Fig. 1)**
CDT-2: anterior to bregma by 1 cm **(Fig. 1)**
CDT-3: posterior to bregma by 1 cm **(Fig. 1)**
CDT-4: inferior to lambda by 1 cm **(Fig. 1)**
CDT-5: Opisthocranion **(Fig. 1)**

On Axial T1

CDT-6: Right euryon **(Fig. 2)**
CDT-7: Left euryon **(Fig. 2)**

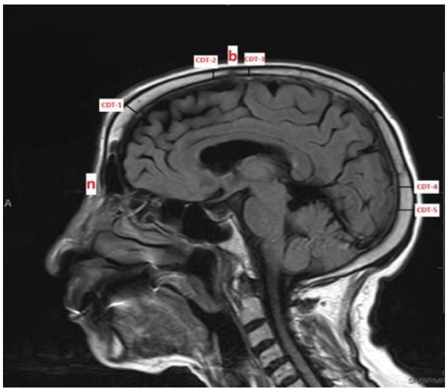

Figure (1): Midsagittal T1 plane of the calvarium showing the assessed points of the Calvarial Diploe Thickness where CDT-1 is the Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b), CDT-2 is the point 1 cm anterior to bregma, CDT-3 is the point 1 cm posterior to bregma, CDT-4 is the point 1 cm inferior to lambda, and CDT-5 is the point at the Opisthocranion (Quoted from Workstation).

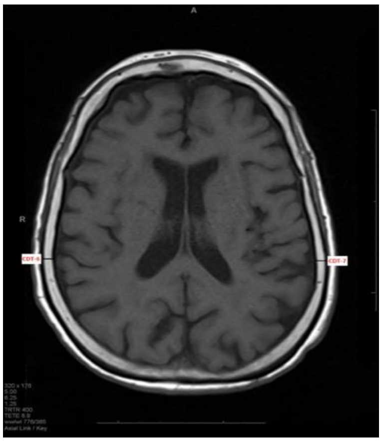

Figure (2): Axial T1 plane of the calvarium showing the assessed points of the Calvarial Diploe Thickness where CDT-6 is the point at the right euryon, and CDT-7 is the point at the left euryon (Quoted from Workstation).

The study was conducted in two stages: The first stage included 256 cranial MRI images. They were equally divided into both sexes. However, equalization was not possible for age. The second stage included 50 cranial MRI images.

Intra- and inter-observer reliability: For intra-observer reliability, 20 cranial MRI images were read by the same observer (Consultant of Diagnostic Radiology) after a 2- week interval and read by two observers (Consultants of Diagnostic Radiology) for inter-observer reliability.

Statistical analysis

Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) version 28.0.0.0 (190) and Microsoft Excel version 16.50. Results with a p-value < 0.05 were considered significant.

For sex estimation: Arithmetic mean and standard deviation were calculated for both males and females, and student's t-test was used for testing the statistical significance between sex and CDT. A logistic regression model assessed sex prediction based on the seven CDT. Receiver Operating Characteristic (ROC) curve analysis was used to assess the logistic regression model by analyzing the area under the curve (AUC). It is drawn for the predicted probabilities and assesses the sensitivity and specificity at the optimal cut-off value, achieving the maximum Youden index, equal to sensitivity+specificity-1 **(Ruopp et al., 2008)**. The developed logistic regression equation for sex estimation was tested on 50 cranial MRI images to assess its accuracy for identifying males, accuracy for identifying females, and overall accuracy.

For age estimation: The sample was divided into five age groups (A=20-<30, B=30-<40, C=40-<50, D=50-<60, E=≥60). Arithmetic mean and standard deviation of CDT measurements for each age group for both sex-stratified and sex-pooled samples were assessed to show the pattern of change of each CDT measurement with increasing age. The degree of association between age and each of the seven CDT measurements was calculated by Pearson's correlation coefficient. Multivariate linear regression model (1) was done for predicting age based on the seven CDT and gender. Multivariate linear regression model (2) was performed for predicting age based on the seven CDT irrespective of gender. The developed multivariate linear regression equations (1) and (2) for age estimation were tested on 50 cranial MRI images to assess the Mean Absolute deviation between the chronological age and predicted age (MAD) and Mean Absolute Percentage Error (MAPE), which indicates the ratio of the error to chronological age.

Intra- and inter-observer reliability: Intraclass correlation (ICC) was done for the seven CDT measurements using the two-way mixed model with the absolute agreement type for single and average measures.

RESULTS

For sex estimation

First stage

Descriptive statistics of the seven measured CDT according to sex: Table 2 shows the mean and standard deviation of the seven measured CDT for both sexes and each sex. Independent student t-test was used to compare CDT between sexes. CDT-2, CDT-3, CDT-4, and CDT-7 were statistically higher in males than females. Only CDT-3 was found to be highly statistically significant between both sexes at the level of $P < 0.001$. CDT-2, CDT-4, and CDT-7 showed statistical significance at $P < 0.05$. Thus, it could be concluded that CDT-2, CDT-3, CDT-4, CDT-7 are significantly sexually dimorphic.

Binary logistical regression model for sex prediction: The seven measured CDT were included in the model, and they jointly succeeded in predicting sex. For Omnibus tests of model coefficients; Chi-Square=103.608, df =7 and $P < 0.001$. Nagelkerke's r^2 was 0.442. Cox & Snell's r^2 was 0.332. The overall classification accuracy of the model was 71.6 %, accuracy for identifying males was 69.5 %, and accuracy for identifying females was 73.6 %. When included in the model, all measured

CDT were statistically significant except for CDT1, CDT5 as shown in table 3. However, their combination in the logistic regression model made the model statistically significant. The beta coefficient was used for developing the binary logistic regression equation for sex prediction. Table 3 shows the beta coefficient, standard error, and significance for each measured CDT. Equation for sex prediction is as follows: Logit = (-3.569) – (0.041*CDT1) + (0.971*CDT2) + (5.129*CDT3) + (0.617*CDT4) – (0.176*CDT5) – (0.984*CDT6) – (4.555*CDT7). A negative logit indicated a female, while a positive logit indicated a male.

$$P(sex)^{*}=1/(1+e^{-(-3.569-0.041*CDT1+0.971*CDT2+5.129*CDT3+0.617*CDT4-0.176*CDT5-0.984*CDT6-4.555*CDT7)})$$

In this model, the cutoff value is 0.5. If the predicted value is ≥0.5 it is male and if it is < 0.5 it is female.

Receiver Operating Characteristic (ROC) curve analysis: Figure 3 shows the plot of the ROC curve (Sensitivity versus 1-Specificity) at all predicted possibilities to assess the performance of the logistic regression model for the sex prediction (Ruopp et al., 2008). Our model had a ROC curve with a high AUC of about 0.816, indicating that the logistic regression model significantly predicts sex. The sensitivity and specificity of the logistic regression model were assessed at the optimal cut-off point 0.46, which achieved the maximum Youden index. Sensitivity was 76.6 %, specificity was 70.5%, as shown in table 4

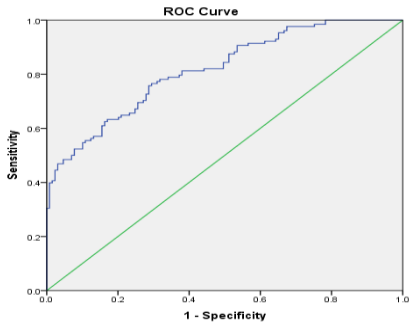

Figure (3): Receiver-operating characteristic curve representing the predicted possibilities generated from the logistic regression analysis for sex prediction

Table (2): Descriptive statistics of the seven measured Calvarial Diploe Thickness measured in mm for each sex

CDT	Total (n=256) Mean±SD	Sex: Male (n = 128) Mean±SD	Sex: Female (n= 128) Mean±SD	t	p
CDT-1	4.04 ± 0.91	4.05 ± 0.91	4.04 ± 0.92	0.086	0.931
CDT-2	2.62 ± 0.67	2.76 ± 0.65	2.47 ± 0.67	3.464*	0.001*
CDT-3	2.28 ± 0.59	2.56 ± 0.54	2.00 ± 0.51	8.499**	<0.001**
CDT-4	4.85 ± 0.85	5.00 ± 0.84	4.70 ± 0.83	2.892*	0.004*
CDT-5	4.60 ± 0.96	4.51 ± 0.88	4.69 ± 1.03	1.558	0.120
CDT-6	2.34 ± 0.42	2.34 ± 0.42	2.34 ± 0.43	0.053	0.958
CDT-7	2.32 ± 0.44	2.37 ± 0.37	2.26 ± 0.49	2.153*	0.032*

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
t: Independent Student t-test
p: p-value for comparison between sex and calvarial diploe thicknesses
: Statistically significant at p ≤ 0.05** *: Statistically significant at p < 0.001**

Table (3): Binary logistic regression model for predicting sex

CDT	B	Standard Error	Wald	p
CDT-1	-0.041	0.171	0.056	0.812
CDT-2	0.971	0.303	10.301	0.001*
CDT-3	5.129	1.420	13.040	<0.001*
CDT-4	0.617	0.195	10.011	0.002*
CDT-5	-0.176	0.160	1.211	0.271
CDT-6	-0.984	0.484	4.131	0.042*
CDT-7	-4.555	1.603	8.073	0.004*
Constant	-3.569	2.018	3.127	0.077

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
B: Beta coefficient ***: Statistically significant at p ≤ 0.05**

Table (4): Agreement (sensitivity, specificity) for the logistic regression model with sex

	AUC	p	95% C.I	Cut off#	Sensitivity	Specificity
Model	0.816	<0.001*	0.766 – 0.867	0.464847	76.6%	70.5%

AUC: Area Under a Curve CI: Confidence Intervals
***: Statistically significant at p ≤ 0.05** **#Cut off was chosen according to maximum Youden index**

<u>Second stage</u>

The resultant binary logistic regression equation for sex prediction showed accuracy for identifying males (78.2 %), accuracy for identifying females (70.4 %), and overall accuracy (74 %).

For age estimation

<u>First stage</u>

The mean age of the studied sample was 40.13± 11.14, and the age range was 20-62 years.

Descriptive statistics of the seven CDT according to age groups: Different five age groups (A=20-<30, B=30-<40, C=40-<50, D=50-<60, E=≥60) were assessed. There were 62 cranial MRI images of participants aged 20-<30, 55 aged 30-<40, 80 aged 40-<50, 52 aged 50-<60, and 7 aged ≥60. Table 5 shows the mean and standard deviation of the seven measured CDT according to age groups. The CDTs weren't uniformly changing with age (Table 5). There were no statistically significant differences between CDT means of different age groups as determined by one-way analysis of variance (ANOVA) and the Welch test. On the other hand, table 6 shows mean and standard deviation of the seven measured CDT according to age groups and sex. CDT-1, for males it increased with age till age group B then decreased till group D then it increased again at group E, while for females it decreased with age till age group B then increased at group C then it decreased again till group E. CDT-2, for males it increased with age till age group C then decreased till group E, while for females it decreased with age till age group C then increased at group D then it decreased again at group E. CDT-3 for males, it increased with age till age group C then decreased till group E, while for females they decreased with age till age group D then increased at group E. CDT-4, for males it increased with age till age group D then decreased at group E, while for females it increased with age till age group C then decreased till group E. CDT-5, for males it decreased with age till age group C then increased at group D then decreased at group E, while for females it increased with age till age group C then decreased till group E. CDT-6, for males it decreased with age till age group B then increased at group C then decreased till group E, while for females it decreased with age till age group C then increased till group E. CDT-7, for males it increased with age till age group D then decreased with age for group E, while for females it decreased with age for all groups.

Pearson correlation used to assess the association between age and CDT showed no statistically significant correlation for sex-pooled sample and males. However, only CDT-3 and CDT-7 showed a statistically significant correlation with age for females (Table 7).

Multivariate linear regression model (1) for age prediction: The variables entered in the model were the seven measured CDT and gender. The model wasn't statistically significant (**P= 0.401**). r^2 of the model was 0.033 showing very small effect size. The model only explained 3 % of the variance, adjusted r^2 was 0.001, standard error of estimate was 11.136. Only the "Gender" was found as a significant predictor for age at **p <0.05**. Table 8 shows the beta coefficient, , standard error, significance for each measured CDT. Equation for prediction of age: Age= (40.507) + (CDT1*0.349) + (CDT2*0.714) + (CDT3*-0.973) + (CDT4*0.442) + (CDT5*-0.571) + (CDT6*-0.553) + (CDT7*-0.633)+ (Gender*3.638) where Gender is 1 for male and 0 for female

When gender is unknown, as in some forensic cases, another multivariate linear regression model (2) was to be considered. The variables entered in the model were only the seven measured CDT irrespective of gender. r^2 of the model was very low (0.014), adjusted r^2 was -0.014, standard error of estimate was 11.219. The model was insignificant (**P= 0.825**). Table 9 shows the beta coefficient, standard error, significance for each measured CDT. Equation for prediction of age irrespective of Gender: Age= 38.654+ (CDT1*0.307) + (CDT2*1.324) + (CDT3*0.643) + (CDT4*0.880) + (CDT5*-0.672) + (CDT6*-1.066) + (CDT7*-1.458)

Table (5): Descriptive statistics of the seven measured Calvarial Diploe Thickness measured in mm for each age group in the sex-pooled sample

CDT	Age Groups A=20-<30 n=62 Mean± SD.	B=30-<40 n=55 Mean± SD.	C=40-<50 n=80 Mean± SD.	D=50-<60 n=52 Mean± SD.	E=≥60 n=7 Mean± SD.	Sig.
CDT-1	3.99 ± 0.96	4.04± 0.81	4.12± 0.91	3.96 ±0.97	4.22 ± 1.05	0.834 [a]
CDT-2	2.57± 0.57	2.54 ± 0.67	2.71 ± 0.78	2.62 ± 0.62	2.59 ±0.70	0.717 [b]
CDT-3	2.24 ± 0.51	2.34 ± 0.63	2.28± 0.61	2.26 ± 0.61	2.50± 0.68	0.774 [a]
CDT-4	4.73± 0.79	4.91± 0.82	4.92± 0.85	4.88± 0.95	4.38± 0.64	0.376 [a]
CDT-5	4.66 ±0.92	4.57 ± 0.92	4.58 ±1.01	4.61± 1.00	4.45 ±1.00	0.973 [a]
CDT-6	2.35±0.35	2.33± 0.43	2.34± 0.47	2.36± 0.43	2.22± 0.40	0.934 [b]
CDT-7	2.33 ± 0.43	2.36± 0.43	2.29± 0.44	2.29± 0.49	2.33 ±0.42	0.914 [a]

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
[a] Statistical Significance between the means of CDT of different age groups, assessed by one-way ANOVA.
[b] Statistical Significance between the means of CDT of different age groups, assessed by Welch test as homogeneity of variance assumption was violated. ***: Statistically significant at p ≤ 0.05**

Table (6): Descriptive statistics of the seven measured Calvarial Diploe Thickness measured in mm for each age group in the sex-stratified sample

CDT	Age groups									
	A=20-<30, n=62		**B=30-<40, n=55**		**C=40-<50, n=80**		**D=50-<60, n=52**		**E=≥60, n=7**	
	Female Mean ± SD.	Male Mean ± SD.	Female Mean± SD.	Male Mean ± SD.	Female Mean± SD.	Male Mean ± SD.	Female Mean± SD.	Male Mean ± SD.	Female Mean± SD.	Male Mean ±SD.
CDT-1	4.13 ±0.97	3.76 ±0.93	3.94 ±0.81	4.15 ±0.80	4.11 ±0.95	4.13 ±0.88	3.89 ±0.94	4.00 ±1.00	3.55 ±1.22	4.22 ±1.05
CDT-2	2.56 ±0.61	2.59 ±0.53	2.43 ±0.70	2.65 ±0.64	2.41 ±0.74	3.00 ±0.70	2.50 ±0.64	2.69 ±0.61	2.47 ±0.25	2.59 ±0.70
CDT-3	2.15 ±0.52	2.37 ±0.48	2.08 ±0.57	2.60 ±0.58	1.93 ±0.45	2.63 ±0.56	1.77 ±0.41	2.57 ± 0.51	2.02 ±0.48	2.50 ±0.68
CDT-4	4.60 ±0.72	4.94 ±0.87	4.82 ±0.79	4.99 ±0.86	4.83 ±0.87	5.02 ±0.83	4.50 ±0.98	5.12 ±0.87	4.16 ±1.08	4.38 ±0.64
CDT-5	4.49 ±0.93	4.93 ±0.85	4.68 ±0.92	4.45 ±0.93	4.86 ±1.04	4.30 ±0.90	4.85 ±1.26	4.46 ±0.77	3.85 ±1.32	4.45 ±1.00
CDT-6	2.35 ±0.36	2.34 ±0.34	2.34 ±0.46	2.32 ±0.40	2.29 ±0.45	2.39 ±0.49	2.43 ±0.47	2.33 ±0.41	2.47 ±0.25	2.22 ±0.40
CDT-7	2.36 ±0.47	2.28 ±0.36	2.35 ±0.48	2.37 ±0.38	2.20 ±0.49	2.38 ±0.35	2.07 ±0.53	2.43 ±0.41	2.02 ±0.48	2.33 ±0.42

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**

Table (7): Correlation between age and Calvarial Diploe Thickness in both sex-pooled and sex-stratified samples

CDT	**Total (n=256)**			**Males**		**Females**	
	Mean ± SD. (mm)	**r**	**p**	**r**	**p**	**r**	**p**
CDT-1	4.04 ± 0.91	0.033	0.602	0.083	0.352	-0.017	0.846
CDT-2	2.62 ± 0.67	0.052	0.407	0.073	0.410	-0.031	0.729
CDT-3	2.28 ± 0.59	0.026	0.673	0.123	0.168	-0.240	0.006*
CDT-4	4.85 ± 0.85	0.049	0.430	0.017	0.851	0.042	0.634
CDT-5	4.60 ± 0.96	-0.062	0.326	-0.152	0.088	0.046	0.606
CDT-6	2.34 ± 0.42	-0.003	0.958	-0.048	0.587	0.046	0.610
CDT-7	2.32 ± 0.44	-0.023	0.717	0.151	0.089	-0.185	0.036*

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
r: Pearson correlation coefficient ***: Statistically significant at p ≤ 0.05**

Table (8): Multivariate linear regression model (1) for age prediction

CDT	B	Std. Error	t-value	p-value	95% Confidence interval		Collinearity Tolerance	VIF
					Lower Bound	Upper Bound		
CDT-1	0.349	0.772	0.452	0.651	-1.171	1.869	0.977	1.024
CDT-2	0.714	1.310	0.545	0.586	-1.865	3.293	0.622	1.609
CDT-3	-0.973	1.609	-0.605	0.546	- 4.143	2.196	0.533	1.876
CDT-4	0.442	0.881	0.502	0.616	-1.293	2.178	0.866	1.155
CDT-5	-0.571	0.742	-0.770	0.442	-2.033	0.890	0.954	1.048
CDT-6	-0.553	2.010	-0.275	0.783	- 4.512	3.406	0.671	1.489
CDT-7	-0.633	1.935	-0.327	0.744	- 4.444	3.178	0.668	1.497
Gender	3.638	1.672	2.176	0.031*	0.345	6.932	0.690	1.449
Constant	40.507	8.691	4.661	0.000	23.390	57.624		

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
B: Unstandardized beta coefficient ***: Statistically significant at p ≤ 0.05**
Std. Error: Standard error
VIF: Variance Inflation factor

Table (9): Multivariate linear regression model (2) for age prediction irrespective of gender

CDT	B	Std. Error	t-value	P-value*	95% Confidence interval		Collinearity Tolerance	VIF
					Lower Bound	Upper Bound		
CDT-1	0.307	0.777	0.396	0.693	-1.223	1.838	0.978	1.023
CDT-2	1.324	1.289	1.027	0.305	-1.214	3.862	0.651	1.535
CDT-3	0.643	1.438	0.447	0.655	-2.190	3.476	0.677	1.476
CDT-4	0.880	0.864	1.018	0.310	-0.823	2.582	0.913	1.095
CDT-5	-0.672	0.746	-0.901	0.369	-2.141	0.798	0.958	1.044
CDT-6	-1.066	2.011	-0.530	0.597	-5.027	2.895	0.681	1.469
CDT-7	-1.458	1.912	-0.763	0.446	-5.223	2.307	0.695	1.439
Constant	38.654	8.714	4.436	0.000	21.492	55.816		

CDT: Calvarial Diploe thicknesses
CDT-1: Midfrontal point, at the midpoint of the direct distance from nasion (n) to bregma (b) on Midsagittal T1
CDT-2: 1 cm anterior to bregma on Midsagittal T1 **CDT-3:1 cm posterior to bregma on Midsagittal T1**
CDT-4: 1 cm inferior to lambda on Midsagittal T1 **CDT-5: Opisthocranion on Midsagittal T1**
CDT-6: Right euryon on Axial T1 **CDT-7: Left euryon on Axial T1**
B: Unstandardized Beta coefficient
***: Statistically significant at p ≤ 0.05**
Std. Error: Standard error
VIF: Variance Inflation factor

Second stage

The age range for the test sample was 20-62 years. Multivariate linear regression equation (1) showed MAD between chronological age and predicted age of 9.09254 years, and

MAPE of 28.458%. Multivariate linear regression equation (2) showed MAD of 8.94469 years; and MAPE of 27.9829%.

Intra- and inter-observer reliability: ICC was 1.000 for intra-observer agreement for all CDT measurements except for CDT-6 and CDT-7 (0.999). ICC (single measures) was 0.995 for inter-observer agreement for CDT-1, 0.994 for CDT-2, CDT-3, and CDT-4, 0.990 for CDT-5, 0.974 for CDT-6 and 0.979 for CDT-7. ICC (average measures) was 0.997 for inter-observer agreement for

CDT-1, CDT-2, CDT-3, and CDT-4, 0.995 for CDT-5, 0.987 for CDT-6 and 0.990 for CDT-7.

DISCUSSION

Lynnerup et al., 2005 recommended a more widespread integration of MRI in forensic research to attain full assessment of the skull diploe dimensions as in some instances, the outline separating the compact bones of the outer and inner cranial vault tables and the cancellous diploe may be questionable **(Lynnerup et al., 2005).** MRI is radiologically well known for its objectivity and non-operator dependence, which offers a favorable diagnostic power owing to its multiplanar images of high resolution. Additionally, its non-ionizing nature renders MRI more desirable for forensic and ethical reasons **(Dedouit et al., 2012; Ruder et al., 2014; Aalders et al., 2017).** Additionally, measuring cranial bone thickness is currently of growing interest for either neurosurgical or plastic surgical purposes. Getting these measurements through sagittal and axial plane T1-weighted MRI images is a fast maneuver that will take less than 5 minutes **(Hatipoglu et al., 2008).**

Unquestionably, developing population-based standards to estimate the biological profile for that studied population is fundamental **(Franklin et al., 2016).** Accordingly, we considered applying the MRI-based CDT assessment on a sample of the Egyptian population to aid in developing reference data for that population. In our study, sex and age were estimated based on seven CDT measurements. All parameters were measured on sagittal and axial plane T1-weighted MRI images.

Since Lynnerup et al., 2005; Sabanciogullari et al., 2013 concluded a high correlation between total cranial thickness (diploe, external and internal tables) and CDT. They also declared that the CDT covaries with the total thickness **(Lynnerup et al., 2005; Sabanciogullari et al., 2013).** We thought it would be of great value to compare our study results to previous studies assessing the CDT as well as the total Calvarial Thickness.

For sex estimation

The present study revealed that CDT-2, CDT-3, CDT-4, and CDT-7 were significantly sexually dimorphic. The significant sexual dimorphism provided support for creating models for sex estimation.

A 2014 study by Santos et al. looked at the best statistical methods for determining sexual dimorphism based on craniometrics. They deemed logistic regression to be the most effective strategy for quickly identifying predictive factors and distinguishing variables. **(Santos et al., 2014).** Therefore, we included the seven measured CDT measurements in a binary logistic regression model as their combination made the model statistically significant with an overall classification accuracy of 71.6 %, accuracy for identifying males was 69.5 %, and accuracy for identifying females was 73.6 %. Moreover, our model had a ROC curve of high AUC, a sensitivity of 76.6 %, and a specificity of 70.5%. Testing the resultant binary logistic regression equation revealed overall accuracy (74%), accuracy for identifying males (78.2 %), and accuracy for identifying females (70.4 %).

Our results regarding the sexual dimorphism of the studied CDT measurements contradict others. Sabancıoğulları et al. 2012 conducted their study on 305 mid-Anatolian patients who performed cranial MRI at Sivas Numune Hospital MRI Unit. The CDT measurements we used were the same as theirs. Except for the CDT-1 and CDT-5 points, they found that CDT was much greater in men **(Sabancıoğulları et al., 2012).** Furthermore, Ishida and Dodo (1990) used a spreading caliber to measure the CVT directly. They concluded that women have much larger frontal and parietal eminences in modern Japanese than men **(Ishida and Dodo, 1990).** The results of these studies differ from ours as we denoted that all CDT points were higher in males except for CDT-5 and CDT-6. The Hatipoglu et al. 2008 study involved 179 Caucasian patients who had MRI scans. Only in the glabella area was there a statistically significant difference in CDT between males and females **(Hatipoglu et al., 2008).** CDT was assessed in 64 people by Lynnerup et al. in 2005 (their autopsy was done at the Institute of Forensic Medicine, University of Copenhagen). They discovered that males had a thicker diploe in general, although this discovery is only statistically significant in the frontal area. **(Lynnerup et al., 2005).** The 2016 study by De Boer et al. looked at the relationship between Cranial Vault Thickness and gender. Frontal cranial thickness (FCT), lateral cranial thickness (LCT), and occipital cranial thickness (OCT) were assessed on 1097 autopsies at Netherlands Forensic Institute (NFI). Only the thickness of the frontal bone revealed substantial sexual dimorphism in their findings **(De Boer et al., 2016).** The results of the previous studies differ from ours as in our study; more CDT measurements were significantly sexually dimorphic.

Other previous studies considered no sexual dimorphism at all for Calvarial Vault thickness or CDT, which disagrees with our results. Concerning Lynnerup's 2001 study, the author concluded that cranial thickness was of little use in sexing humans **(Lynnerup, 2001)**. Baral et al. (2013) considered Nepalese calvaria to be devoid of sexual dimorphism, claiming that no significant differences between males and females were identified in the entire sample **(Baral et al., 2013).** Such differences could be attributed to the difference in the populations assessed, the use of different measurement points, or other modalities.

For age estimation

Our study revealed that CDT wasn't uniformly changing with age for all the measured CDT. Pearson correlation shows no statistically significant correlation between age and all studied CDT measurements. The multivariate linear regression models for age prediction; model (1) that included the seven measured CDT and gender and model (2) that included the seven measured CDT irrespective of gender, weren't statistically significant with very low r^2, very low adjusted r^2, and high standard error of estimate. Testing the resultant multivariate linear regression equations showed MAD of 9.09254 years; MAPE of 28.458% for the multivariate linear regression equation (1) and MAD of 8.94469 years; and MAPE of 27.9829% for the multivariate linear regression equation (2). Including the gender in the multivariate linear regression model (1) has increased both the MAD and the MAPE compared to not including it in the model (2), denoting that sex-specific reference data did not improve the age estimation when using the MRI-based CDT assessment.

Our results concerned with age estimation are in accordance with most previous studies for different populations, which showed the absence of correlation, or existence of only very faint trends, between cranial thickness or CDT and age. The relationship between cranial vault thickness and age was investigated by De Boer et al. in 2016. Their findings revealed no significant relationship between cranial vault thickness and age in individuals of both sexes. They concluded that using cranial vault thickness measurements to draw deliberate postulations on any component of the biological profile is nearly impossible **(De Boer et al., 2016).** According to the findings of Lynnerup's 2001 study, the author concluded that cranial thickness in aged human remains is unworthy **(Lynnerup, 2001).** Ishida and Dodo 1990 could not find any correlation between diploic thickness and age **(Ishida and Dodo, 1990).** The lack of a correlation between CDT and age might be explained by the theory that CDT is unaffected by diploic bone resorption, which happens as people become older as the diploic bone is replaced by fatty marrow **(Hatipoglu et al., 2008).**

On the contrary, Hatipoglu et al. 2008 found a statistically significant linear correlation between age and diploe thickness using MRI. They also concluded the possibility of identifying age based on the CDT **(Hatipoglu et al., 2008).** According to

Sabancoullar et al. (2012), the CDT varies with age. From the age of 61 and up, CDT increased **(Sabancıoğulları et al., 2012).** Sabanciogullari et al., 2013 conducted an MRI study to measure CDT at eight points. They denoted a positive linear correlation between CDT and age except for opisthocranion, right euryon, and 1cm inferior to lambda **(Sabanciogullari et al., 2013)**. The findings of prior research are not the same as ours. This may be due to the difference in the populations assessed or the use of different measurement points.

The inconsistent findings of certain prior research done in various populations demonstrated the importance of adopting population-based criteria **(Franklin et al., 2016)**. As a result, our findings are significant because we contemplated using an MRI-based CDT evaluation on a sample of Egyptians to help in the development of reference data for that group.

CONCLUSION

We concluded that CDT could be included as a new candidate in MRI-based sex estimation for Egyptians. On the other hand, this was not favorable for age estimation.

RECOMMENDATIONS

- Due to the misclassification regarding age-based MRI assessment of CDT, the presented method needs to be studied further on a greater sector of the Egyptian population.
- We also recommend future studies to compare the accuracy of other imaging modalities in estimating age using the presented CDT measurements.
- Further studies to assess age estimation in the living using MRI-based methods are recommended.
- Studying other bones for sex and age estimation should be increased to ensure a successful forensic identification process.

Conflicts of interest

The authors declare that they have no conflicts of interest.

REFERENCES

Aalders, M.C., Adolphi, N.L., Daly, B., Davis, G.G., de Boer, H.H., Decker, S.J., et al. (2017): Research in forensic radiology and imaging; Identifying the most important issues. Journal of Forensic Radiology and Imaging, 8:1–8.

Al-Khatieeb, M.M. (2011): Sexual Dimorphism of Calvarial Thickness Parameter in Different Skeletal Patterns. Mustansiria Dental Journal, 8(2):8.

Baral P, Koirala, S., and Gupta, MK (2013): Calvarial Thickness of Nepalese skulls-Computerised Tomographic (CT) study. Anatomy & Physiology, 04(02).

Carew, R.M. and Errickson, D. (2019): Imaging in forensic science: Five years on. Journal of Forensic Radiology and Imaging, 16:24–33.

Clemente, M.A., Tegola, L.L, Mattera, M. and Guglielmi, G. (2017): Forensic Radiology: An Update. Journal of the Belgian Society of Radiology, 101(S2):21.

De Boer, H.H. (Hans), Van der Merwe, A.E. (Lida) and Soerdjbalie-Maikoe, V. (Vidija) (2016): Human cranial vault thickness in a contemporary sample of 1097 autopsy cases: relation to body weight, stature, age, sex, and ancestry. International Journal of Legal Medicine, 130(5):1371–1377.

Dedouit, F., Auriol, J., Rousseau, H., Rouge', D., Crube'zy, E., and Telmonet, N. (2012): Age assessment by magnetic resonance imaging of the knee: A preliminary study. Forensic Science International, 217(1–3): 232.e1-232.e7.

Farzana, F., Shah, B.A., Shahdad, S., Zia ul Haq, P., Sarmast, A., and Ali, Z. (2018): Computed tomographic scanning measurement of skull bone thickness: a single-center study. International Journal of Research in Medical Sciences, 6(3).

Fortes de Oliveira, O., Lima Ribeiro Tinoco, R.; Daruge Júnior, E., Silveira Dias Terada, A.S., Alves da Silva, R.H., and Paranhos, L.R. (2012): Sexual Dimorphism in Brazilian Human Skulls: Discriminant Function Analysis. Journal of Forensic Odontostomatology, 30(2): 26–33.

Franklin, D., Swift, L. and Flavel, A. (2016): "Virtual anthropology" and radiographic imaging in the Forensic Medical Sciences. Egyptian Journal of Forensic Sciences, 6(2): 31–43.

Grabherr, S., Baumann, P., Minoiu, C., Fahrni, S., and Mangin, P. (2016): Post-mortem imaging in forensic investigations: current utility, limitations, and ongoing developments. Research and Reports in Forensic Medical Science, 6: 25–37.

Guglielmi, G., Nasuto, M., and Pinto, A. (2015): Forensic and medicolegal radiology: challenges, issues, and new perspectives. La radiologia medica, 120(9): 777–778.

Hatipoglu, H.G., Ozcan, H.N., Hatipoglu, U.S., and Yuksel E. (2008): Age, sex and body mass index in relation to calvarial diploe thickness and craniometric data on MRI. Forensic Science International, 182(1–3): 46–51.

Higginbotham-Jones, J. and Ward, A. (2014): Forensic radiology: The role of cross-sectional imaging in virtual post-mortem examinations. Radiography, 20(1): 87–90.

Ishida, H. and Dodo, Y. (1990): Cranial thickness of modern and Neolithic populations in Japan. Human Biology, 62(3):389–401.

Kalim, Z., and Tyagi, R. (2018) 'Sex Determination Using Canine Dimorphism: Forensic Relevance, Journal of Forensic Sciences & Criminal Investigation, 11(1).

Lynnerup, N. (2001): Cranial thickness in relation to age, sex, and general body build in a Danish forensic sample. Forensic Science International, 117(1–2): 45–51.

Lynnerup, N., Astrup, J.G. and Sejrsen, B. (2005): Thickness of the human cranial diploe in relation to age, sex, and general body build. Head & Face Medicine, 1(1).

Mallett, X., Blythe, T., and Berry, R. (2014): Advances in Forensic Human Identification. 1st edition, CRC Press; 271-288.

Neumayer, B., Schloegl, M., Payer, C., Widek, T., Tschauner, S., Ehammer, T., et al. (2018): Reducing acquisition time for MRI-based forensic age estimation. Scientific Reports, 8:2063.

Ruder, T.D., Thali, M.J. and Hatch, G.M. (2014): Essentials of forensic post-mortem MR imaging in adults. The British Journal of Radiology, 87: 20130567.

Ruopp, M.D., Perkins, N.J., Whitcomb, B.W., and Schisterman E.F. (2008): Youden Index and Optimal Cut-Point Estimated from Observations Affected by a Lower Limit of Detection. Biometrical Journal, 50(3): 419–430.

Sabancıoğulları, V., Kos¸ar, M.I., S¸alk, I., Erdil, F.H., O¨ztoprak, I., and C¸imen, M. (2012): Diploe thickness and cranial dimensions in males and females in mid-Anatolian population: An MRI study. Forensic Science International, 219: 289.e1-289.e7.

Sabancıoğulları, V., Salk, I. and Cimen, M. (2013): The Relationship between Total Calvarial Thickness and Diploe in the Elderly. International Journal of Morphology, 31(1): 38–44.

Santos, F., Guyomarc'h, P. and Bruzek, J. (2014): Statistical sex determination from craniometrics: Comparison of linear discriminant analysis, logistic regression, and support vector machines. Forensic Science International, 245: 204.e1-204.e8.

Spradley, M.K. (2016): Metric Methods for the Biological Profile in Forensic Anthropology: Sex, Ancestry, and Stature. Academic Forensic Pathology, 6(3): 391–399.

Yasar Teke, H., Ünlütürk, O., Günaydin, E., Duran, S., and Özsoy, S. (2018): Determining gender by taking measurements from magnetic resonance images of the patella. Journal of Forensic and Legal Medicine, 58: 87–92.

الرنين المغناطيسي لسمك طبقة العظم الإسفنجي لقبة القحف لتقدير الجنس والعمر لعينة من المصريين

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المقدمة: الرنين المغناطيسي (MRI) أصبح مرغوبًا فيه في سياق الطب الشرعي وذلك لطبيعته غير المؤينة ولدقته وحساسيته. وتعد الجمجمة، واحدة من أكثر الأجزاء العظمية التي تم استخدام جوانبها المورفولوجية لفترة طويلة لتقدير كل من الجنس والعمر. وعلى الرغم من ذلك فلا يزال مدى إمكانية استخدام قياس طبقة العظم الإسفنجي لقبة القحف (CDT) لتقدير الجنس و العمر قيد البحث. لذلك هدفت هذه الدراسة إلى معرفة ما إذا كان يمكن تقدير الجنس والعمر بناءا على سمك طبقة العظم الإسفنجي لقبة القحف باستخدام الرنين المغناطيسي في عينة من المصريين. **المواد والطرق:** أجريت الدراسة على صور الرنين المغناطيسي على الجمجمة ل 306 مصريين بالغين لتقدير الجنس والعمر، تم قياس سمك طبقة العظم الإسفنجي في سبعة مناطق لقبة القحف (CDT1-7) على 256 صورة بالرنين المغناطيسي للجمجمة معروفة الجنس والعمر ثم تم اجراء تحليلات إحصائية للقياسات السبع ثم تم إعداد معادلة انحدار لوجستي ثنائي لتقدير الجنس ومعادلتين الانحدار الخطي متعدد المتغيرات لتقدير العمر. ولإنشاء معادلات تقدير العمر؛ المعادلة (1)، تم تضمين الجنس، في حين أن المعادلة (2) كانت بغض النظر عن الجنس. تم اختبار جميع المعادلات على 50 صورة بالرنين المغناطيسي للجمجمة. **النتائج**: أظهر اختبار معادلة تقدير الجنس دقة في التعرف على الذكور (78.2٪) ودقة في التعرف على الإناث (70.4٪) ودقة عامة (74٪). فيما يتعلق بتقدير العمر، أظهر ارتباط بيرسون عدم وجود علاقة ذات دلالة إحصائية بين العمر وجميع قياسات السبع. كانت نماذج الانحدار الخطي متعددة المتغيرات الخاصة بالتنبؤ بالعمر غير ذات دلالة إحصائية. **الاستنتاج:** خلصت الدراسة إلى أن قياسات CDT المدروسة يمكن إدراجها كمرشح جديد في تقدير الجنس القائم على التصوير بالرنين المغناطيسي للمصريين، ولكن ذلك لا ينطبق على تقدير العمر. تقدم نتائجنا نتائج أولية لتقييم نهج جديد لتقدير الجنس والعمر للمصريين. يوصى بشدة بتطبيق مثل هذه المعايير على قطاع أكبر من المصريين لكل من تقدير الجنس والعمر وكذلك استخدام طرق أشعة مختلفة ومقارنتها بالرنين المغناطيسي.