

Cranial Characteristics, Maxillofacial, and Skull Base Structure of Non-Human Primate (Adult *Macaca fascicularis*): A Preliminary Study for Cranial Craniotomy Model

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Abstract

The use of non-human primate (NHP) animal models, which anatomical and physiological similarities to human, is important for the sake of learning the anatomical properties. This study aimed to characterize the cranial, maxillofacial, and skull base structures of non-human primates as a potential model suitable for a cranial craniotomy model. Adult *Macaca fascicularis* (MF) skulls classified as specific pathogen-free for TB, SIV, SV40, Polio, Foamy virus and Herpes B virus from PT Bio Farma (Persero) Animal Lab. Library were used to represent the anatomical model. The open access database from Mammalian Crania Photographic Archive 2nd Edition (MCPA2) was used for cranial characterization analysis. This study was performed at the Department of Neurosurgery, Dr. Hasan Sadikin General Hospital and the Animal Laboratory of PT. Biofarma (Persero) from November 2018 to January 2019. The skull base structures were assessed for its analogies with its human counterpart. Comparison by *t-student* analysis between male and female skulls shows the mean male cranial length (CL) is greater than in female (116.68 vs 102.50 mm), with $p=0.000$; the mean male bizygomatic width (BZB) is greater than in female (79.30 vs 69.70 mm) with $p=0.001$; the mean male posterior cranial breadth (CBN) is greater than in female (63.40 vs 58.79 mm) with $p=0.019$; and the mean male cranial base length (CBL) is greater than in female (63.32 vs 57.55 mm), with $p=0.001$. The skull of MF is suitable for Neurosurgery and Neuroscience study since the MF cranial characterization and structure are similar to that of human. Its structure is ideal for performing craniotomy since it has several characteristics such as cranial vault, maxillofacial structure with huge temporal muscle, and skull base structure.

Key words: Cranial measurement, maxillofacial and skull base structure, non-human primate

Karakteristik Kranium, Maksilofasial, dan Struktur Dasar Tengkorak *Non-human Primate Macaca fascicularis* dewasa: Studi Pendahuluan untuk Model Craiotomi Kranium

Abstrak

Penggunaan hewan model berasal dari primata bukan-manusia (NHP), dimana secara anatomis dan fisiologis mirip dengan manusia, sangat penting untuk dapat mempelajari struktur anatominya. Penelitian ini bertujuan untuk karakterisasi struktur kranium, maksilofasial dan dasar tengkorak primata (*Non-human Primate*) yang berpotensi sebagai model penelitian kraniotomi. Tengkorak dewasa *Macaca fascicularis* (MF) dari Laboratorium Hewan PT Biofarma (Persero), bebas infeksi TBC, SIV, SV40, Polio, Foamy Virus, dan Herpes B digunakan sebagai model anatomi. Basis data terbuka *Mammalian Crania Photographic Archive 2nd Edition* (MCPA2) digunakan untuk analisis kranium. Penelitian dilakukan di Departmen Bedah Saraf RSHS dan Laboratorium Hewan PT. Biofarma pada November 2018–Januari 2019. Struktur tengkorak MF dipelajari analogi seperti pada struktur tengkorak manusia. Analisis *uji-t* tengkorak jantan dan betina menunjukkan rerata panjang kranial (Cranial length, CL) jantan lebih panjang dibanding betina (116.68 vs 102.50 mm, $p=0.000$); rerata *bizygomatic width* (BZB) jantan lebih panjang dibanding betina (79.30 vs 69.70 mm, $p=0.001$); rerata *posterior cranial breadth* (CBN) jantan lebih panjang dibanding betina (63.40 vs 58.79 mm, $p=0.019$); dan rerata *cranial base length* (CBL) jantan lebih panjang dibanding betina (63.32 vs 57.55 mm, $p=0.001$). Tengkorak MF sesuai untuk berbagai penelitian bidang bedah saraf dan neurosains. Karakterisasi kranial dan strukturnya sama dengan yang dimiliki manusia. Struktur kranium MF merupakan model ideal untuk kraniotomi berdasar karakteristik tulang tengkorak, otot temporal besar pada maksilofasial, dan struktur dasar tengkorak.

Kata kunci: Pengukuran kranium, *non-human primate*, struktur maksilofasial dan dasar tengkorak

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Introduction

The use of non-human primate (NHP) animal models is important for the sake of learning *in vivo* phenomenon, given its biological and anatomical properties are closely related to human primate counterpart. NHP has anatomical and physiological similarities to human that results of research in NHP will have significant relevance to humans (Figure 1), particularly in medicine field.¹ Members of the European Parliament conservation status based on the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) includes the NHP in Appendix II category, which means that these animals can be traded without damaging their survival by not retrieving them directly from their natural habitat as well as by following the international trade regulations and monitoring the trade in these animals.² The *Macacafascicularis* skulls are similar to other species of Macaque in their anatomical landmark.³ This study used the NHP *Macacafascicularis* (MF) skulls to characterize the cranial, maxillofacial, and skull base structures to assess their potential suitability as a cranial craniotomy model.

Methods

This study was approved by the Ethics Committee of the Institutional of Animal Care and Use Ethics Commission (IACUC) of PT Bio Farma (Persero) through the issuance of the ethical clearance No. 01/IACUC-BF/III/2017 with a validity period of 2 years, i.e. between April 14, 2017 to 2019. This study was performed at the Department of Neurosurgery, Dr. Hasan Sadikin General Hospital and the Animal Laboratory of PT.Biofarma (Persero) during December 2018 to January 2019.

The specimens of adult *Macacafascicularis* skull (Figure 2A-C) belong to PT. Biofarma (Persero) Animal Lab and were taken from healthy donors (male, free from specific pathogens such as TB, SIV, SV40, Polio type 1,2,3, Foamy virus, and Herpes B virus).

Data on NHP cranium shown in Table 1 were obtained from the Mammalian Crania Photographic Archive Second Edition (MCPA2), as revised on December 1, 2005, as accessed at http://1kai.dokkyomed.ac.jp/mammal/en/species_all/macaca_fascicularis.html. Each NHP cranium, which was placed horizontally, was photographed from 6 different angles (anterior,

posterior, left, right, superior, and inferior) at a long distance using a camera with telephoto or telemacro lens. The long-distance shot decreases perspective distortion that lead to measurement errors when studying cranial profiles. For the cranial images in which the anatomical direction was deviated from the lens' optical axis due the technical inaccuracy, adjustments were applied repeatedly in the 3D rotations on the cranium's anatomical axes until the setting error was minimized. No digital enhancement was applied in image capture where the results were saved in a JPG compressed format at 6 megapixel resolution. The high resolution images enable specific observation of characteristics in details and comparisons of images on a computer screen. Cranial length (CL) was defined as maximum length of neurocranium in the mid sagittal plane, which measured using a caliper from nasion. Zygomatic breadth was defined as bizygomatic width (BZB) from zygion to zygion while posterior cranial breadth was defined as maximum breadth width at lateral nuchal line (CBN). Furthermore, nasion to basion was defined as cranial base length (CBL) from anatomical landmark of nasion in front of basion in the skull base. These measurements are illustrated in Fig.3A, B.

Results

Based on Table 1, there were 24 adult MF specimens, comprised of 15 male (62.5%) and 9 female (37.5%) specimens. There were 1.67 times more male than female MF crania measured in our study.

The overall shortest cranial length (CL) size was 98.9 mm (DKY_2616) and the longest was 131.5 mm (DKY_2678). Meanwhile, the shortest and the longest bizygomatic widths (BZB)(DKY_1556) were 64 mm and 92.2 mm (DKY_2678), respectively. It was also revealed that the shortest posterior cranial breadth (CBN) was 55.1 mm (DKY_1057) while the longest was 72.3 mm (DKY_0989). The shortest cranial base length (CBL) was 50 mm (DKY_2047) while the longest was 69 mm (DKY_2829).

In adult MF males, the shortest CL size was 105.2 mm (DKY_2447) and the longest was 131.5 mm (DKY_2678), with the mean \pm standard deviation (SD) of 116.7 ± 7.8 , as shown in Table 2 while the shortest BZB was 66.9 mm (DKY_1057) and the longest was 92.2 mm (DKY_2678), with mean of 79.3 ± 6.45 . Next, the shortest CBN was 55.1 mm (DKY_1057) and the longest was 72.3

Table 1 Specimen Code (Sex, Adult) from MCPA2 Database (see Material Methods for detail)

MF Identity	Sex	Measurements (mm)			
		Maximum Length (CL)	Zygomatic Breadth (BZB)	Posterior Cranial Breadth (CBN)	Nasion -Basion (CBL)
DKY_0727	Male	119.4	80.4	66.7	64.0
DKY_0989	Male	131.3	90.3	72.3	65.0
DKY_0995	Male	121.5	83.4	67.3	67.4
DKY_1057	Male	107.5	66.9	55.1	56.0
DKY_1229	Female	106.0	72.4	58.2	57.9
DKY_1556	Female	101.6	64.0	56.2	56.0
DKY_2008	Male	114.6	79.5	66.3	63.7
DKY_2047	Female	100.1	67.6	55.9	50.0
DKY_2122	Female	102.9	67.6	57.5	60.8
DKY_2447	Male	105.2	72	56.5	57.9
DKY_2581	Male	109.2	75.3	60.5	60.8
DKY_2614	Female	104.0	71.8	62.3	59.7
DKY_2615	Female	105.4	77.1	63.4	59.5
DKY_2616	Female	98.9	71.6	59.0	58.3
DKY_2630	Male	117.7	78.6	63.1	63.9
DKY_2646	Male	121.5	77.2	62.9	66.4
DKY_2678	Male	131.5	92.2	71.8	N/A
DKY_2829	Male	111.1	81.8	61.9	69.0
THK_0177	Female	99.0	67.1	57.7	58.1
THK_0923	Female	104.6	68.1	58.9	57.7
THK_1342	Male	110.9	76.1	63.3	60.2
THK_1345	Male	112.4	74.2	58.1	58.0
THK_1371	Male	116.1	81.8	65.3	66.0
THK_1372	Male	120.4	79.9	59.9	66.5

mm (DKY_0989), with a mean of 63.45 while the shortest CBL was 56 mm (DKY_1057) and the longest was 69 mm (DKY_2829), with a mean of 63.2 ± 3.9 .

In adult MF females, the shortest CL size was 98.9 mm (DKY_2616) and the longest was 105.4 mm (DKY_2615), with the mean of 102.5 ± 2.72 as shown in Table 2 while the shortest BZB was 64 mm (DKY_1556) and the longest was 72 mm (DKY_1229), with a mean of 69.7 ± 3.88 . Furthermore, the shortest CBN was 55.9 mm (DKY_2047) and the longest was 63.4 mm (DKY_2615), with a mean of 58.8 ± 2.5 while the shortest CBL was 50 mm (DKY_2047) and the longest was 60.8 mm (DKY_2122), with a mean of ± 3.1 .

When comparing male vs female measurements, it was discovered that the mean male CL was greater than that of females (116.68 vs 102.50) and the difference was significant ($p=0.000$). A significant difference ($p=0.001$) was also found between the mean male and female BZB where the male one was greater than the female one (79.30 vs 69.70). Other significant differences were also seen between the mean male and female CBN (63.40 vs 58.79), in which the male one was greater, as greater than female ($p=0.019$) and between the male and female CBL where the male one was greater (63.32 vs 57.55) ($p=0.001$).

The primary bones of the maxillofacial structures are maxilla, mandible, small frontal

Table 2 Cranial Characteristics of 24 Specimens of Adult *Macaca Fascicularis*

Cranial Characteristics (n=24 (Adult))	Mean in mm ± standard deviation
Maximum Length (CL)	
Male (25)	116.7±7.8
Female (9)	102.5±2.72
Zygomatic Breadth (BZB)	
Male (25)	79.3±6.45
Female (9)	69.7±3.88
Posterior Cranial Breadth (CBN)	
Male (25)	63.4±5
Female (9)	58.8±2.5
Nasion-Basion (CBL)	
Male (25)	63.2±3.9
Female (9)	57.6±3.1

bone, nasal bone, and zygoma and the primary bones that constructs the facial bones are one vomer, two maxilla bones, one mandible, two nasal bones, two palatine bones, two lacrimal bones, two zygomatic bones and two nasal concha bones (Figure 2AB).

The skull base structure is divided into 3

areas: (i) anterior fossa, (ii) middle fossa, and (iii) posterior fossa. The bones that primarily constructs the skull base are frontal bone, sphenoid bone, temporal bone, and occipital bone. In details, the skull base is constructed of the crista galli, ethmoid bone, roof of orbita, sella turcica, lesser wing of sphenoid bones, petrous bones, and the posterior wall of petrous bones (Figure 2C).

Discussion

Macacafascicularis, also known as long-tailed monkeys, cynomolgus, or crab-eating monkeys, is native to Southeast Asia (Indonesia, Philippines and Malaysia). These monkeys are found throughout Indonesia such as in Java, Sumatra, Bali and Kalimantan. These monkeys live in groups, with the dominance of male monkeys as group leaders. MF’s main habitats are mangrove areas, coastal areas, and forests up to 2000 meters above sea level.^{3,4}

MF has the ability to see using both eyes at the same time (binocular vision) and it has a muscular tail that is covered by short hairs. The length of this species’ tail usually ranges from 400–565 mm. Head and body length of *Macacafascicularis* ranges from 350 to 455 mm. In relation to the animal models used in this study, the Macaque brain is also protected by a skull and three covering layers that are very

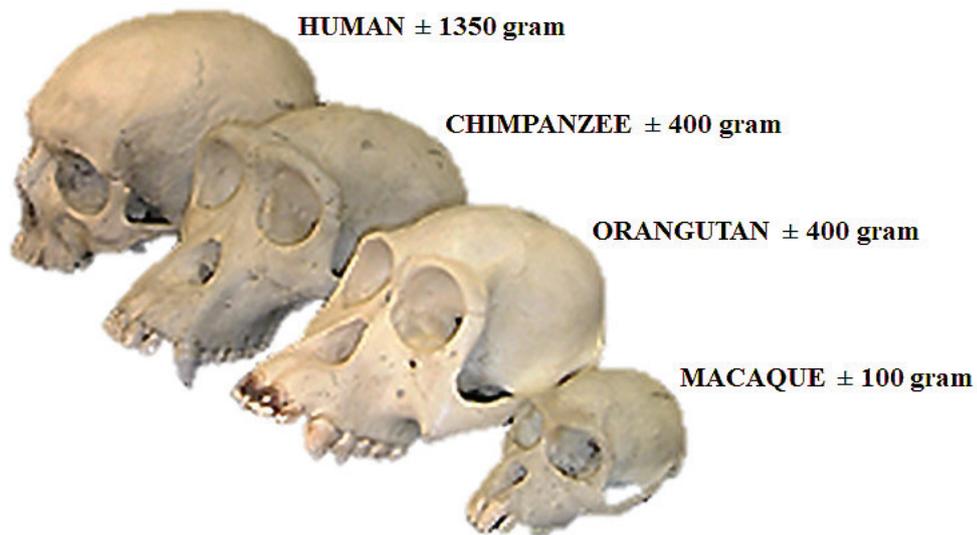


Figure 1 Comparable Size and Weight between g Human Primate Brain and Its Non-Human Primate Counterpart. Figure Shows the Size and Weight of Human, Chimpanzee, Orangutan, and Macaque Species Skulls



Figure 2 Photograph of An Adult *Macacafascicularis* Skull; Anterior (A); Sagittal (B); and Axial Views that Expose the Skull Base Structures (C)

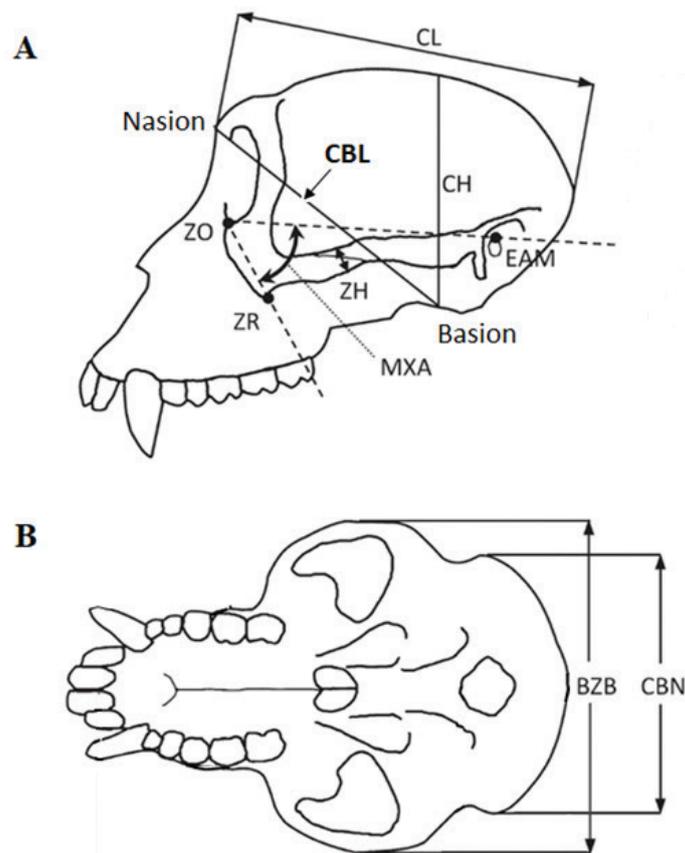


Figure 3 Illustration of The Cranial Length (CL), Bizygomatic Width (BZB), Cranial Breadth Nuchal Line (CBN) and Cranial Base Length (CBL)

Cranial height (CH) from basion to bregma. Zygomatic height (ZH) at temporozygomatic suture (TZS) minimum distance measured from superior zygomatic process to inferior temporal process across middle TZS. Maxillary angle (MXA): the angle taken between the length from zygomaticomaxillary suture (ZMS) at inferior orbital margin (ZO) to ZMS at root of zygomatic arch (ZR) and the length from ZMS at inferior orbital margin (ZO) to the middle of the external auditory meatus at the upper margin of the meatus (EAM).

strong. The layers are, from the outside to inside, duramater, arachnoid, and pyramid layers. The duramater is composed of solid collagen connective tissue.⁴

It was suggested in a previous study that the cranial length of MF species, specifically *Macaca fuscata*, is between 100.5 mm to 119.4 mm in adult female MF whereas in the male counterparts, the length is 118.6 mm to 133.1 mm.³ The weight of the Macaque brain tissue is around 100 grams.⁵ MF has the same anatomical and physiological structures as humans. The visual complex and motoric control in Macaque have the same physiological and anatomical control as humans.⁵

Previous study indicates that the cranial dimensions can show age-related changes with an increasing pattern from young adulthood (7.0 years) to mid-adulthood (13.3–19.0 years in males and 19.7–22.6 years in females) and then become stagnant from mid-adulthood to very old age (26.9 years or more) or increasing from young adulthood to very old age.^{6,8} This study only used young adulthood macaques with the following results: the male CL is significantly greater than female (116.68 vs 102.50; $p=0.000$); the mean male BZB is significantly greater than the female (79.30 vs 69.70; $p=0.001$); the mean male CBN is significantly greater than female (63.40 vs 58.79; $p=0.019$); and the mean male CBL is also significantly greater than that of females (63.32 vs 57.55; $p=0.001$). Collectively, this shows that cranial dimensions in male *Macaca fascicularis* is greater than those of its female counterpart, which is similar to human beings.^{7,8,11,12}

As for maxillofacial bones and skull base structures, a complete maxillofacial primary bones are observed in *Macaca fascicularis*, i.e. maxillae, mandible, small frontal bone, nasal bone, and zygoma along with complete skull base primary bones consisting of frontal bone, sphenoid bone, temporal bone, and occipital bone.^{9,10,13} Therefore, its structures are ideal for performing craniotomy since it has several characteristics, such as the cranial vault, maxillofacial regions with huge temporal muscle, and skull base structures that resemble the anatomical structure of human-primate.^{9,11,12} The skull houses and protects the brain and sensory organs, supports critical functions, and provides a framework onto which muscles and other soft tissue can attach to.^{15,16} Even the histological structures of human meninges layer that consist of duramater, arachnoid, and piamater are also found in MF.^{8,16} Soft tissue structures are also present within the cranium, such as the dural

septa (tentorium cerebelli, falxcerebri, and falxcerebelli) and septal cartilage. It has been suggested that these structures may play a functional and important roles in craniofacial form.^{14,15,16}

Cranial anatomy has a central role in studies of systematics, phylogeny, and functional anatomy in primate and human.¹² In conclusion, this study found that the MF skull is a miniature scale of human skull that its functional anatomy is suitable for neurosurgery and neuroscience studies.

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