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NOTE

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Body surface area measurements in male Hartley guinea pigs using a computed tomography scanner

Tadashi ITOH[1)]*, Mifumi KAWABE[2)], Takahiko NAGASE[1)], Katsumi ENDO[1)], Masafumi MIYOSHI[3)] and Kazuro MIYAHARA[3)]

[1)]Nihon Bioresearch Inc., 6-104 Majima, Fukujucho, Hashima, Gifu 501-6251, Japan
[2)]Animal Medical Center, Faculty of Applied Biological Sciences, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
[3)]Veterinary Medical Center, Obihiro University of Agriculture and Veterinary Medicine, Inadacho, Obihiro, Hokkaido 080-8555, Japan

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ABSTRACT. The body surface area (BSA) of animals is generally estimated by multiplying the *k* value (constant) by the measured body weight (BW) raised to the power of 2/3 (Meeh's formula). Computed tomography (CT) scanners generate detailed 3-dimensional (3D) images of objects, and image analysis does not depend on operator skill. Therefore, the analysis of CT images provides accurate and reproducible BSA measurements. In this study, we measured the BSA of 25 male Hartley guinea pigs from 3 to 36 weeks of age (working BW range: 0.233 to 1.160 kg) using a CT scanner and 3D analysis software. We concluded that the *k* value for male Hartley guinea pigs was 8.37, based on the mean *k* value of the 25 animals.

KEY WORDS: body surface area, computed tomography (CT), CT scanner, guinea pig, Hartley

Guinea pigs are one of the most commonly used laboratory animals. For example, the non-clinical study methods using male guinea pigs were published for skin sensitization in 1959 [3], and for photosafety evaluation in 1970 [19]. Even today, the guidelines for chemical testing issued by the Organization for Economic Cooperation and Development (OECD) recommend guinea pigs for repeated dose dermal toxicity [15, 16] and skin sensitization [17]. The guideline issued by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) for photosafety evaluation describes study methods using guinea pigs [7]. The Hartley guinea pig is the most famous outbred breed of laboratory guinea pig and has been used in many non-clinical studies. On the other hand, the guinea pig's size, gentle nature, and coat variety make it a popular companion and hobby animal. Additionally, humans valued this animal as an important food source. To this day guinea pigs are considered as a delicacy in many areas [2]. Therefore, guinea pigs are very important species in veterinary medical sciences.

The body surface area (BSA) of an organism is an important parameter for evaluating physiological functions. BSA has also been used as a criterion for drug dosage determination in clinical [18]. In drug development, normalization of a dosage by BSA (i.e., conversion of a dosage from mg/kg to mg/m^2) is an appropriate method for extrapolating doses between species. The Food and Drug Administration (FDA) Center for Drug Evaluation and Research guidance recommends the use of BSA to estimate starting doses in the initial clinical trials for therapeutics in volunteer subjects [4]. Thus, accurately determined BSA of animals is extremely important. Especially in laboratory animals, accurate BSA is necessary to interpret and extrapolate the test results obtained with each species. The BSA of animals has generally been estimated by multiplying a constant (k) by the measured body weight (BW) raised to the power of 2/3 [13]. The k values (100 × BSA [m^2]=k × BW [kg]$^{2/3}$, i.e., Meeh's formula) reflect the density and body shape of the animals. The k values for various animal species have been determined from the measured BSA and BW. To date, the k values for guinea pigs have been calculated from the BSA measured using traditional methods. Spector [20] reported k values using skinning and triangulation (k=7.1 to 10.4), Hong *et al*. [6] (2/N guinea pigs, k=8.054) and Liu *et al*. [12] (male strain 13 guinea pigs, k=9.17 to 11.31) used skinning, and Fougère and Wynn [5] did not mention the method of BSA determination (k=10.5). However, it has been pointed out that the accuracy and reproducibility of these traditional methods have limitations [8].

Computed tomography (CT) scanners generate detailed 3-dimensional (3D) images of objects, and image analysis does not depend on operator skill. Therefore, the analysis of CT images provides accurate and reproducible BSA measurements. Miyoshi, one of the authors of this note, published the BSA measurement method for animals using a CT scanner and 3D analysis software

*Correspondence to: Itoh, T.: ito.tadashi@nisshin.com

[14]. Previously, we determined the BSAs of laboratory miniature pigs and rabbits using this measuring method. The *k* values were calculated for peripubertal- or mature-miniature pigs, juvenile miniature pigs, New Zealand White rabbits, and male Japanese White rabbits as 7.98 [8], 8.58 [9], 11.0 [10], and 14.602–0.959 × BW (kg) [11], respectively. In this study, we measured the BSA of male Hartley guinea pigs from CT images and calculated the *k* value.

Hartley guinea pigs (Kwl:Hartley) were obtained from Kiwa Laboratory Animals Co., Ltd., Wakayama, Japan. The BSA was measured for 25 male guinea pigs that were used in other non-clinical studies and euthanized by anesthesia with sodium pentobarbital according to the protocols of those studies. As shown in Table 1, the BWs and ages ranged from 0.233 to 1.160 kg (mean: 0.757 kg, median: 0.731 kg) and from 3 to 36 weeks (mean: 17.8 weeks, median: 14.0 weeks), respectively. No critical abnormalities in clinical signs or BW changes were noted. All studies were conducted in compliance with the Guidelines for Management and Welfare of Experimental Animals of Nihon Bioresearch Inc.

The BSA was measured as described previously [9]. Briefly, the body of each guinea pig was set in the prone position for whole-body CT scanning on the day of euthanasia. Images were obtained using a multislice CT scanner (Alexion TSX 033A, Toshiba Medical Systems Co., Ltd., Tochigi, Japan, tube voltage: 120 kV, tube current: 150 mA, helical pitch: 5.5). The slice thickness and reconstruction interval were 2 mm and 1 mm, respectively. The BSA of each animal was determined from the 3D CT images (Fig. 1) using high-speed 3D analysis software (TRI-3D/VOL, Ratoc System Engineering Co., Ltd., Tokyo, Japan) based on the computer graphics algorithm, Marching Cubes and Discriminant Analysis Method. The *k* value was back-calculated from the BSA and BW.

As shown in Table 1, the measured BSAs ranged from 0.0334 to 0.0902 m^2. The mean ± standard deviation (SD), coefficient of variation (CV), and median for the *k* value were 8.37 ± 0.30, 3.64%, and 8.24, respectively. The reported, standard BW values of weaning guinea pig ranged from 0.15 to 0.20 kg and standard BW values of male adult guinea pig from 0.9 to 1.0 kg [2]. According to Charles River Technical Bulletin, BW values of male Hartley guinea pigs at breeding retirement age (20 months old) ranged from 1.0 to 1.2 kg [1]. Therefore, the BWs of the 25 males used were distributed across the standard BW range. The *k* value variation was limited due to a small CV. We concluded that the *k* value for male Hartley guinea pigs was 8.37, based on

Table 1. Body weight (BW), age, measured body surface area (BSA), *k* value, calculated BSA, and calculated BSA/measured BSA in male Hartley guinea pigs

	BW (kg)	Age (week)	Measured BSA (m^2)	*k* value	Calculated BSA (m^2)*	Percentage**
	0.233	3	0.0334	8.82	0.0317	94.9
	0.379	7	0.0462	8.82	0.0438	94.8
	0.437	7	0.0515	8.94	0.0482	93.6
	0.451	7	0.0527	8.96	0.0492	93.4
	0.499	7	0.0541	8.60	0.0527	97.4
	0.515	7	0.0560	8.72	0.0538	96.1
	0.613	11	0.0596	8.26	0.0604	101.3
	0.642	11	0.0616	8.28	0.0623	101.1
	0.657	11	0.0644	8.52	0.0633	98.3
	0.709	30	0.0697	8.77	0.0666	95.6
	0.713	14	0.0654	8.19	0.0668	102.1
	0.728	11	0.0667	8.24	0.0677	101.5
	0.731	14	0.0658	8.11	0.0679	103.2
	0.741	14	0.0664	8.11	0.0685	103.2
	0.812	30	0.0738	8.48	0.0728	98.6
	0.841	20	0.0737	8.27	0.0746	101.2
	0.886	14	0.0742	8.04	0.0772	104.0
	0.890	36	0.0758	8.19	0.0774	102.1
	0.912	30	0.0770	8.19	0.0787	102.2
	0.969	30	0.0804	8.21	0.0820	102.0
	1.067	20	0.0847	8.11	0.0874	103.2
	1.100	20	0.0863	8.10	0.0892	103.4
	1.120	36	0.0868	8.05	0.0903	104.0
	1.125	20	0.0874	8.08	0.0905	103.5
	1.160	36	0.0902	8.17	0.0924	102.4
Mean	0.757	17.8	0.0682	8.37		
SD	0.254	10.5	0.0143	0.30		
CV				3.64%		
Median	0.731	14.0	0.0667	8.24		

*: 100 × the calculated BSA (m^2)=8.37 × BW $(kg)^{2/3}$. **: 100 × the calculated BSA (m^2)/the measured BSA using a CT scanner (m^2). SD: standard deviation, CV: coefficient of variation.

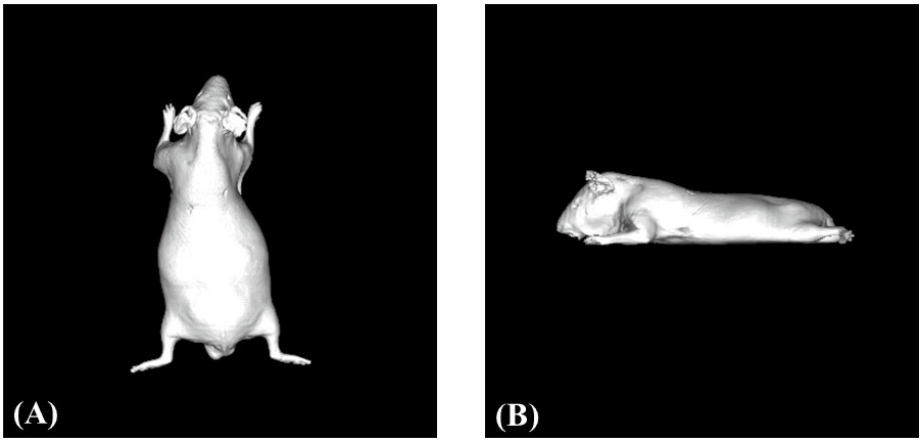

Fig. 1. Computed tomography (CT) images of male Hartley guinea pig. (A) Hartley guinea pig in dorsal aspect. (B) In lateral side.

the mean *k* value of the 25 animals. The percentages of the calculated BSAs with the *k* value (8.37) to the measured BSAs using a CT scanner ranged from 93.4 to 104.0%. Therefore, the error of this estimation formula is small. We propose that this accurate and reproducible measuring method be used to verify the *k* values of other species, especially laboratory animals. Furthermore the *k* values should be compared between species, breeds, and gender to interpret and extrapolate the test results of non-clinical studies.

CONFLICT OF INTEREST. The authors declare that there is no conflict of interest.

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