Scandinavian Journal of Laboratory Animal Science

2017, Volume 43, Number 2
ISSN 2002-0112

Original scientific article

Determination of Body Surface Area in Japanese White Rabbits

*By L Bai[1,2], B Huang[1,2], Y Chen[1,2], S Zhao[1,2], J Fan[3], E Liu[1,2 *]*

[1]Research Institute of Atherosclerotic Disease, Cardiovascular Research Center, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi 710061, China
[2]Laboratory Animal Center, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi 710061, China
[3]Department of Molecular Pathology, Interdisciplinary Graduate School of Medicine and Engineering, University of Yamanashi, Yamanashi 409-3898, Japan

[*]Correspondence: Professor, Director Enqi Liu
Research Institute of Atherosclerotic Disease,
Xi'an Jiaotong University Cardiovascular Research Center,
Xi'an, Shaanxi 710061, China
Tel: +86-29-82657057
Fax: +86-29-82655362
E-mail: liuenqi@mail.xjtu.edu.cn

Summary

Accurate calculation of body surface area (BSA) is essential for many biomedical applications and conversion of drug doses among various species. In this study, forty Japanese white rabbits with a body weight of 2.5-3.0 kg were used to determine a precise formula and practical method for BSA calculation. Rabbit BSA was measured two ways: by coating with a kraft paper or by skin stripping, followed by calculation of the surface area planometrically. We compared the BSA data from these two methods and found there was no difference. The BSA data were subsequently entered into the Meeh's formula (BSA $=kW^{2/3}$), the most commonly used for experimental animals, to calculate the mean k constant from coating (11.35) and stripping (11.30). Furthermore, the K_m factor, which is commonly used for dose translation based on BSA between human and animals, was calculated based on the formula (BSA=body weight (kg)/ K_m factor). The K_m factor from coating and stripping was 12.38 and 12.40, respectively. In conclusion, coating is an easy and accurate way to measure rabbit BSA and can replace stripping. We also provide an accurate k constant and K_m factor for Japanese white rabbits.

Introduction

Body surface area (BSA) is a crucial parameter of interest for many reasons including studies of body heat transfer, normalization of physiological responses, administration of drug doses, estimation of burnt skin percentage, calculation of volume of fluid replacement and calculation of nutritional needs (*Crawford et al., 1950; Pinkel, 1958; Freireich et al., 1966; Widdowson, 1983; Vauthey et al., 2002; Gibson et al., 2003*). In clinical practice, the calculations for determining starting dose in humans as extrapolated from animals always use the more appropriate normalization of BSA (*Freireich et al., 1966; Schein et al., 1970; Reagan-Shaw et al., 2008*). Therefore, how to accurately measure BSA in different species is becoming an important issue for both the scientific community as well as the general public.

Various formulae for BSA calculation have been reported in the literature. For humans, a formula based on V (body volume) and L (body length), $BSA=(9\pi VL)^{0.5}$, has been derived (*Wang et al., 2004b; Wang et al., 2004a*). For animals, BSA is conventionally calculated using the Meeh factor (k) times the

body mass scaled to two thirds power (BSA=kW$^{2/3}$) (*Gouma et al., 2012*). However, Meeh factors always vary according to species and size of the animal. Hence, an accurate k constant value is required for each species and weight range (*Gilpin, 1996; Gouma et al., 2012*).

According to guidelines of the US Food and Drug Administration (FDA), the extrapolation of animal dose to human dose is correctly performed only through normalization to BSA, which is represented in mg/m^2 (*Reagan-Shaw et al., 2008*). The K_m factor is used to convert the mg/kg dose to an mg/m^2 dose. The K_m factor can be calculated as body weight (kg) divided by BSA (m^2) (*Reagan-Shaw et al., 2008*). A dose in mg/kg is multiplied by K_m to convert to mg/m^2. The human equivalent dose (HED) can be more appropriately calculated by the formula: HED (mg/kg)=Animal dose (mg/kg)x(Animal K_m/Human K_m) (*Reagan-Shaw et al., 2008*). K_m values vary greatly in different species. For example, the K_m factor for dog is 20, but the K_m factor for mouse is only 3 (*Center for Drug Evaluation and Research, 2002*).

Rabbits are widely used as animal models for various experiments and testing due to being small, usually docile, easily restrained, cheap to maintain and because they breed prodigiously (*Fan et al., 2015; Peng et al., 2015; Csomos et al., 2016*). Owing to the high similarity of lipid metabolism with humans, rabbits are used as a model for human atherosclerosis (*Yanni, 2004; Getz et al., 2012)*. Moreover, rabbits are used to study disorders of the eyes, skin, heart, and immune system, as well as in studies of asthma, cystic fibrosis, diabetes, lung disease and stem cell therapy (*Kamaruzaman et al., 2013; Liao et al., 2015; Peng et al., 2015; Zernii et al., 2015; Kuriyama et al., 2016*). Therefore, determination of rabbit BSA has great significance for many basic biomedical studies and clinical applications. To find an easy way to calculate BSA and establish a more accurate formula, the BSA of Japanese white rabbits was measured using coating and skin stripping. We propose a simple and practical way to calculate BSA and also provide an accurate k constant and K_m factor for Japanese white rabbits.

Materials and methods

Experimental animals

Forty Japanese white rabbits (7-months-old, males), weighing 2.5-3.0 kg, were provided by the Laboratory Animal Center of Xi'an Jiaotong University. The animals were housed individually in cages (RB35-15G, Suhang Sci-technology Company, Suzhou, China). All animals were kept at room temperature 20-22°C, humidity 50-60%, under 12/12h of light/dark conditions. Rabbits were provided *ad libitum* with rabbit chow (Animal Feed Company of Beijing Keao Xieli, Beijing, China) and water. All animal experiments were pre-approved by the Xi'an Jiaotong University Institutional Animal Care and Use Committee, and performed in accordance with National legislation and the Convention ETS 123 (Council of Europe) and the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health.

Coating procedure

Rabbits were weighed and anaesthetized with 10% chloral hydrate dissolved in sterile water (1.5 ml/kg) (Xinyu Biotechnology Company, Shanghai, China) via ear vein injection. A plain, non-slippery piece of kraft paper, which was durable and did not wrinkle with use, was used for coating the rabbits. The length of each rabbit, from nose to anus, was measured and recorded. Firstly, the whole body of rabbit was wrapped up tightly by plastic wrappers with several small holes for breathing (Fig. 1A). Then, the rabbit was placed onto the downside paper, ventral side facing down with tail, front and rear legs hidden below the ventral side, and the ventral surface of the rabbit was marked on the downside paper (Fig. 1B). Subsequently, the upside paper was held very tight and close to the dorsal surface of the rabbit, until it reached the downside paper. Scotch tape was used to seal wrinkles. At this position, the dorsal-lateral surface area of the animal was carefully marked on the coating paper (Fig. 1C). The coating paper was not as flat as the paper which covered the rabbit's torso. In an effort to make sure of the accuracy of the measurement, we divided the coating paper into three parts that is head, buttock and torso. To make sure the head and buttock parts were flat enough for measuring, these parts were cut into several pieces of paper (Fig.1D). After that, the small pieces of paper of head and buttock, and the torso paper, were photographed (Fig.1E). Afterwards, the front leg of the rabbit wrapped with plastic wrappers was placed on the downside paper and marked on the downside paper (Fig. 2A). The coating paper was pressed gently against the downside paper, so that the front leg was enclosed between them (Fig. 2C). The edge was marked on the upside paper (Fig. 2E). The same procedure, as described for the front legs, was used to determine the surface area of the rear legs (Fig. 2B, 2D, 2F), ears (Fig. 3A, 3B) and tail (Fig. 3C, 3D, 3E, 3F). All the pieces of paper were collected and photograp-

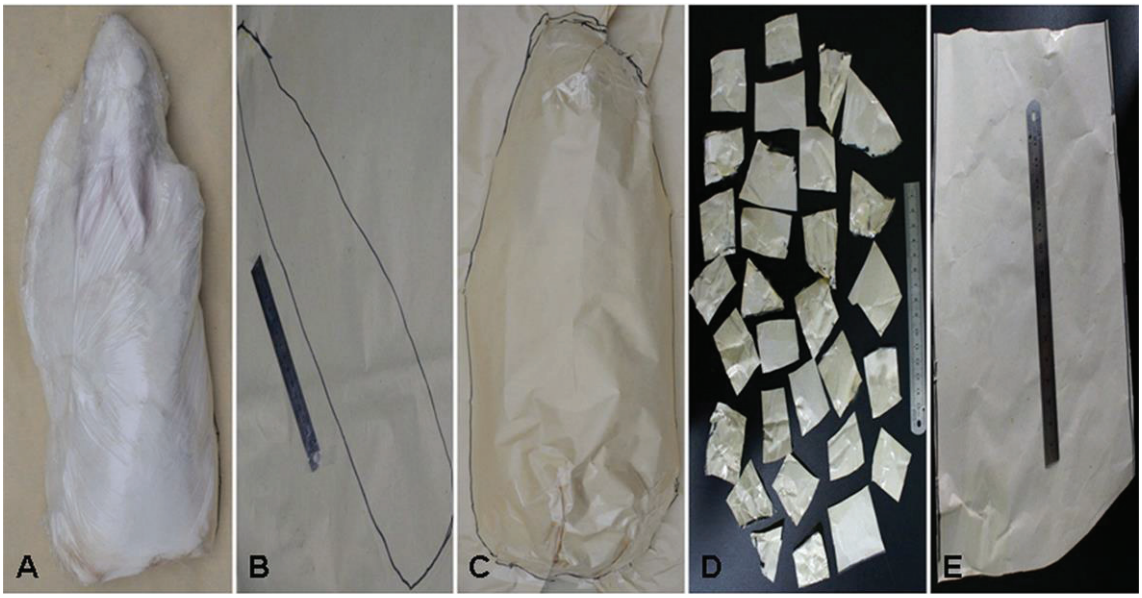

Figure 1. The basic steps of the suggested procedure of BSA measurement in rabbits. A. the rabbit was wrapped with the plastic wrappers and kept ventral side faced down. B. The shape of the ventral surface area was marked on the kraft paper. C. the dorsal-lateral surface area of the rabbit was carefully marked on the coating paper. D. The coating paper was cut into several small pieces. E. The shape of torso area.

hed (Fig. 1D, 1E). The surface area of each part was measured using image analysis software (WinROOF Ver.6.5, Mitani Co., Ltd., Fukui, Japan). The total BSA area was calculated by addition. All rabbits survived this part of the study.

Skinning procedure

After being measured by kraft paper, rabbits were killed by injection of sodium pentobarbital (100mg/kg) via the ear vein, and then skinned. The epidermis of each rabbit was stripped. Then, the stretched pelt was put on a board smoothly and photographed immediately. Rabbit BSA was also measured by WinRoof software.

Statistical analysis

The group sizes were decided by the equation: $N=2+C(S/d)^2$. N, group size; *C*, constant obtained according to α and β; S, standard deviation; *d*, effect size. The statistical power was assumed as 0.9, and α was 0.05. Data are expressed as mean ± SD. A statistically significant difference between means was determined by using the t-test. All statistical procedures were performed using SPSS (SPSS version 13.0, Statistical Package for the Social Sciences software, SPSS, Chicago, IL, USA). Differences were considered statistically significant at $P<0.05$.

Results

BSA and k constant

BSA-1 (0.224) was calculated with data from alive rabbits (Table 1). BSA-2 (0.223) was calculated with data from stripped rabbits (Table 2). The k constant for each rabbit was calculated based on the Meeh's formula ($k=BSA/W^{2/3}$). Mean values for k-1 and k-2 were 11.35 and 11.30, respectively (Table 2). Statistical analysis indicated that there was no significant difference between BSA-1 and BSA-2 ($P=0.69$) (Fig. 4A). The analysis of the deviation showed that it was very small between the BSA values from alive rabbits and stripped rabbits (deviation : +0.4%) (Table 2). The obtained k-1 and k-2 values were also not significantly different ($P=0.30$) (Fig.4B). These results suggest that coating is an effective method for BSA measurement, which can replace the skinning method, and does not require rabbits to be sacrificed.

K_m factor

The K_m factor is used to convert the mg/kg dose used in a study to an mg/m^2 dose. It was calculated using the following formula: K_m factor=body weight (kg)/BSA (m^2). Based on the obtained BSA-1 and BSA-2 data, K_m factor -1 (12.38) and K_m factor -2 (12.42) were obtained (Table 2). There was no significant difference between K_m factor -1 and K_m factor -2 ($P=0.45$) (Fig. 4C), suggesting a reliable K_m value had been obtained using the paper wrapping method.

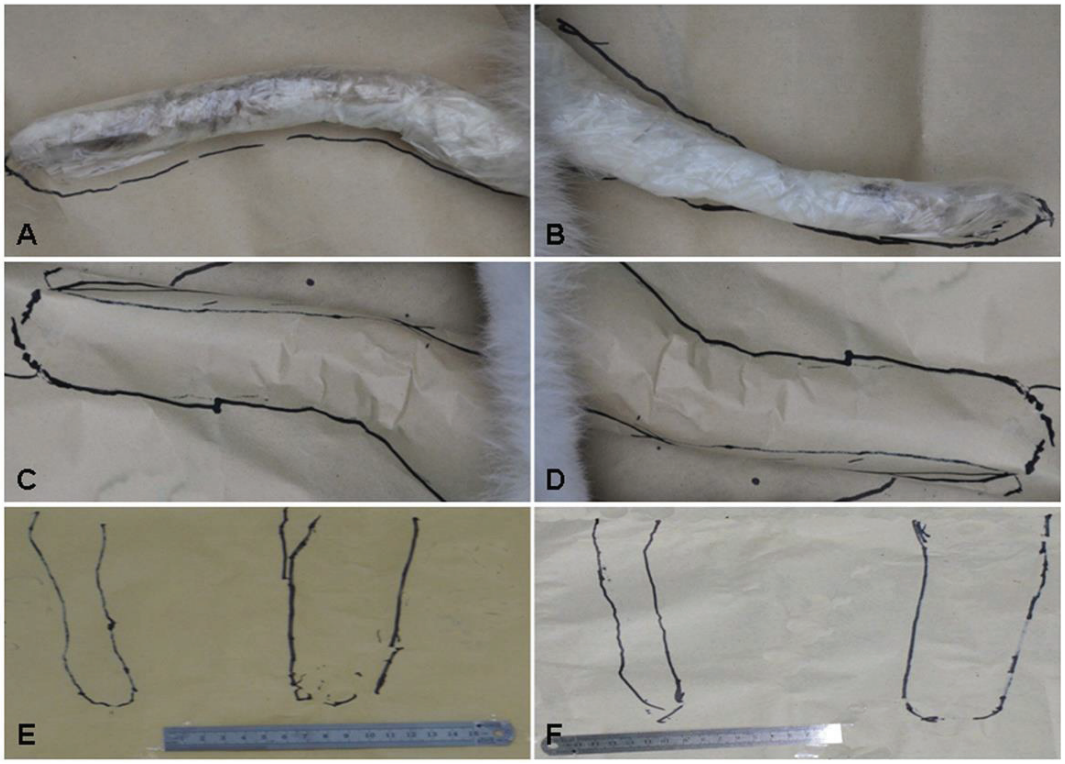

Figure 2. The basic steps of the suggested procedure of leg surface area measurement in rabbits. A. the front leg of the rabbit was wrapped with the plastic wrappers and placed on the kraft paper. B. the rear leg of the rabbit was wrapped with the plastic wrappers and placed on the kraft paper. C. the front leg surface area of the rabbit was carefully marked on the coating paper. D. the rear leg surface area of the rabbit was carefully marked on the coating paper. E. The shape of the front leg surface area was marked on the kraft paper. F. The shape of the rear leg surface area was marked on the kraft paper.

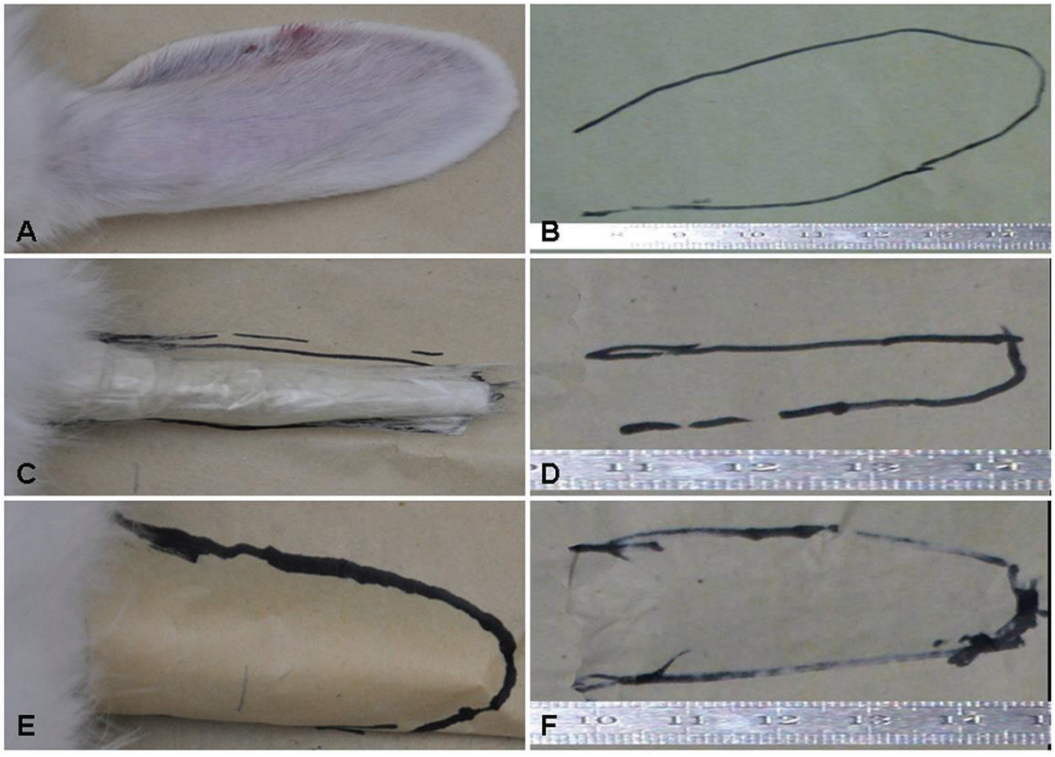

Figure 3. The basic steps of the suggested procedure of ear and tail surface area measurement in rabbits. A. The ear of the rabbit was placed on the kraft paper. B. The shape of the ear surface area was marked on the kraft paper. C. the tail of the rabbit wrapped with the plastic wrappers was placed on the kraft paper (ventral side faced down). D. The shape of the tail surface area was marked on the kraft paper. E. the tail surface area of the rabbit was carefully marked on the coating paper. F. The shape of the tail surface area was marked on the coating paper.

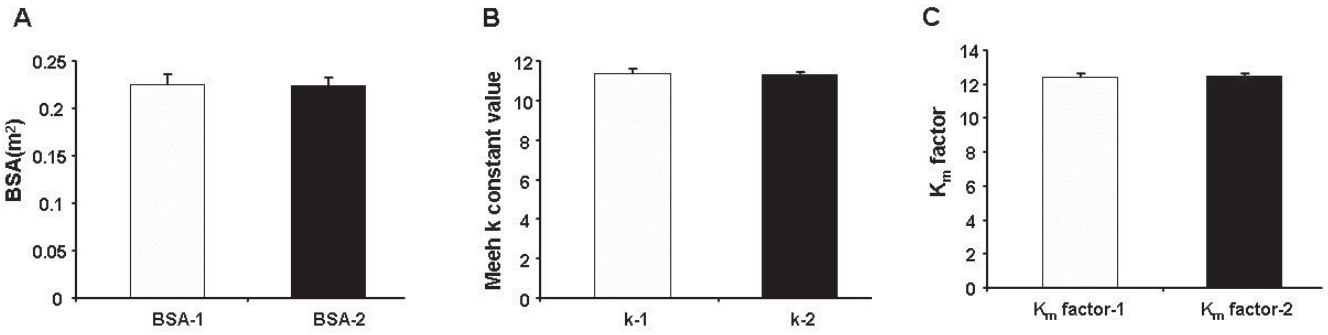

Figure 4. Comparative analysis of BSA, k constant value and K_m factor in rabbits. A. There was no difference between BSA-1 and BSA-2. B. k-1 value from BSA-1 was similar to k-2 value based on BSA-2. C, K_m factor -1 was also similar to K_m factor -2.

Discussion

The rabbit is a widely used animal model both in biomedical and clinical research. The present study establishes an easy and effective way to estimate rabbit BSA, and also provides an accurate Meeh's k constant and K_m factor based on the two different methods. BSA is becoming a key factor for converting a dose from animals to humans, especially for phase I and phase II clinical trials (*Kaestner et al., 2007; Reagan-Shaw et al., 2008*). Currently, BSA-based dose calculation and translation is the most appropriate method, which is far superior to the simple conversion based on body weight. To improve therapeutic outcomes in clinical trials, more appropriate dose conversions are needed.

BSA measurement can be carried out by direct methods, indirect methods and predictive formulae. Direct methods include coating, surface integration, triangulation and three-dimensional whole-body scanning (*Breton et al., 2008; Cheung et al., 2009; Zehnder et al., 2012)*. Indirect methods can be classified as linear geometric and photographic. Predictive formulae are usually generated from population studies (*WangHihara, 2004b; Lee et al., 2008*). These methods for BSA measurement have advantages and disadvantages. Direct methods are more accurate, but usually complex, time-consuming and impractical in both the experimental and clinical setting. Indirect estimation methods are simple and convenient, but have less accuracy. Predictive formulae are derived from many studies using direct methods. Although the predictive formulae are straightforward methods for BSA calculation and have been widely used, their applicability has been frequently questioned due to the diversity of species, weight and strains (*Gilpin, 1996; WangHihara, 2004b; Cheung et al., 2009*).

In the present study, rabbit BSA was calculated using coating and skinning. With a group size of 40 and a standard deviation of 0.012, a significant difference of more than 0.009 could have been shown with a p-value less than 0.05 and a power of 0.9. The BSA data from alive or stripped rabbits were very similar (0.224 ± 0.012 vs. 0.223 ± 0.010). Thus, any real difference is likely to be smaller than this. We presumed that differences were statistically significant at $P < 0.05$. This should be an acceptable confidence limit for the method. Further analysis of the deviation between the BSA values from alive rabbits and stripped rabbits showed that it was quite narrow (deviation: $+0.4\%$), which suggests that skinning can be replaced by coating and there is no need to sacrifice rabbits in future studies. More importantly, coating is a very simple, convenient and easy method which is not only suitable for rabbits but also can be applied to other small or medium laboratory animals.

For mammals, the BSA is usually calculated using Meeh's formula ($BSA=kW^{2//3}$), which is the most commonly used for experimental animals (*Meeh, 1879; Diack, 1930; Gouma et al., 2012*). BSA calculation for domestic rabbits has been reported using CT-guided modelling (*Zehnder et al., 2012*). The k constant was determined to be 9.9 (range, 9.59 to 10) (*Spector, 1956; Zehnder et al., 2012*). In our study, Meeh k values (11.30 and 11.25) for Japanese white rabbits were obtained using two measurement methods. The different k values from these studies may be due to different strains, body weights or ages.

In recent years, BSA has been widely used for conversion of drug doses between different species, especially from animals to humans. The K_m factor, a crucial index, is usually used to convert the mg/kg dose to an mg/m^2 dose (*Center for Drug Evaluation and Research, 2002; Reagan-Shaw et al., 2008*). The K_m values based on average BSA calculations for human, baboon, dog, monkey, rabbit, guinea pig, rat, hamster and mouse have been reported by the FDA (*Center for Drug Evaluation and Research,*

Table 1. BSA data from alive rabbits

Rabbit code	Ventral area (m^2)	Dorsallateral area (m^2)	Tail area (m^2)	Ear area (m^2)	Front leg area (m^2)	Rear leg area (m^2)	BSA-1 *(m^2)	Length (m)	Weight (kg)
1	0.038	0.098	0.004	0.024	0.020	0.027	0.210	0.41	2.76
2	0.041	0.093	0.004	0.017	0.019	0.034	0.209	0.42	2.65
3	0.036	0.101	0.005	0.024	0.027	0.032	0.225	0.43	2.76
4	0.032	0.098	0.005	0.019	0.016	0.038	0.208	0.43	2.54
5	0.048	0.113	0.004	0.028	0.024	0.034	0.251	0.45	3.15
6	0.036	0.094	0.004	0.022	0.022	0.031	0.210	0.43	2.60
7	0.039	0.103	0.004	0.024	0.022	0.031	0.223	0.43	2.75
8	0.042	0.107	0.005	0.025	0.015	0.031	0.225	0.42	2.74
9	0.045	0.112	0.004	0.026	0.018	0.024	0.230	0.43	2.77
10	0.049	0.108	0.004	0.024	0.017	0.029	0.232	0.43	2.80
11	0.047	0.109	0.005	0.027	0.016	0.028	0.231	0.43	2.84
12	0.050	0.111	0.004	0.023	0.018	0.029	0.234	0.44	2.93
13	0.035	0.094	0.004	0.023	0.022	0.029	0.207	0.45	2.53
14	0.037	0.101	0.005	0.026	0.017	0.026	0.212	0.45	2.57
15	0.046	0.102	0.005	0.028	0.024	0.029	0.235	0.46	2.96
16	0.041	0.097	0.005	0.022	0.020	0.032	0.218	0.44	2.69
17	0.039	0.097	0.004	0.023	0.022	0.028	0.213	0.44	2.63
18	0.040	0.097	0.004	0.024	0.022	0.028	0.215	0.43	2.66
19	0.040	0.108	0.004	0.023	0.023	0.025	0.223	0.43	2.83
20	0.045	0.101	0.005	0.025	0.018	0.030	0.224	0.44	2.73
21	0.043	0.115	0.004	0.018	0.021	0.034	0.235	0.43	2.87
22	0.045	0.095	0.004	0.021	0.019	0.028	0.211	0.42	2.63
23	0.050	0.102	0.006	0.023	0.021	0.030	0.232	0.42	2.87
24	0.040	0.122	0.004	0.023	0.018	0.030	0.236	0.43	3.02
25	0.042	0.102	0.004	0.024	0.021	0.030	0.223	0.43	2.72
26	0.046	0.107	0.005	0.024	0.019	0.028	0.229	0.43	2.84
27	0.044	0.110	0.004	0.024	0.019	0.029	0.231	0.43	2.85
28	0.044	0.112	0.004	0.022	0.021	0.029	0.233	0.45	2.92
29	0.045	0.105	0.004	0.022	0.021	0.028	0.225	0.43	2.75
30	0.043	0.113	0.004	0.021	0.021	0.029	0.231	0.45	2.94
31	0.045	0.094	0.004	0.020	0.018	0.026	0.207	0.48	2.55
32	0.045	0.105	0.004	0.023	0.019	0.031	0.228	0.43	2.77
33	0.045	0.110	0.005	0.023	0.021	0.031	0.234	0.43	2.96
34	0.043	0.107	0.005	0.023	0.017	0.026	0.221	0.44	2.75
35	0.039	0.094	0.004	0.023	0.017	0.025	0.202	0.43	2.48
36	0.048	0.122	0.005	0.026	0.021	0.029	0.251	0.44	3.07
37	0.045	0.113	0.005	0.023	0.021	0.029	0.236	0.44	2.96
38	0.045	0.11	0.005	0.024	0.018	0.027	0.229	0.45	2.73
39	0.047	0.114	0.004	0.025	0.016	0.029	0.234	0.44	2.93
40	0.037	0.096	0.004	0.022	0.016	0.026	0.201	0.43	2.51
Mean	0.043	0.104	0.0043	0.023	0.020	0.029	0.224	0.435	2.78
SD	0.004	0.007	0.0003	0.002	0.002	0.003	0.012	0.013	0.16

*BSA-1 was measured when animals were alive. SD, standard deviation.

Table 2. Individually calculated k values and K_m factors using planimetric measurements

Rabbit code	Weight (kg)	BSA-1 *(m^2)	BSA-2 *(m^2)	Deviation (%)	k-1*	k-2*	K_m factor-1*	K_m factor-2 *
1	2.76	0.210	0.214	-1.86916	10.67	10.88	13.14	12.90
2	2.65	0.209	0.213	-1.87793	10.91	11.12	12.68	12.44
3	2.76	0.225	0.224	0.446429	11.44	11.38	12.27	12.32
4	2.54	0.208	0.209	-0.47847	11.17	11.23	12.21	12.15
5	3.15	0.251	0.249	0.803213	11.68	11.59	12.55	12.65
6	2.60	0.210	0.211	-0.47393	11.11	11.16	12.38	12.32
7	2.75	0.223	0.226	-1.32743	11.36	11.51	12.33	12.17
8	2.74	0.225	0.221	1.809955	11.49	11.29	12.18	12.40
9	2.77	0.230	0.227	1.321586	11.66	11.51	12.04	12.20
10	2.80	0.232	0.223	4.035874	11.68	11.23	12.07	12.56
11	2.84	0.231	0.228	1.315789	11.52	11.37	12.29	12.46
12	2.93	0.234	0.232	0.862069	11.43	11.33	12.52	12.63
13	2.53	0.207	0.210	-1.42857	11.15	11.31	12.22	12.05
14	2.57	0.212	0.213	-0.46948	11.30	11.35	12.12	12.07
15	2.96	0.235	0.231	1.731602	11.40	11.21	12.60	12.81
16	2.69	0.218	0.219	-0.45662	11.27	11.32	12.34	12.28
17	2.63	0.213	0.212	0.471698	11.18	11.13	12.35	12.41
18	2.66	0.215	0.216	-0.46296	11.20	11.25	12.37	12.31
19	2.83	0.223	0.222	0.45045	11.15	11.10	12.69	12.75
20	2.73	0.224	0.221	1.357466	11.47	11.31	12.19	12.35
21	2.87	0.235	0.229	2.620087	11.64	11.34	12.21	12.53
22	2.63	0.211	0.213	-0.93897	11.07	11.18	12.46	12.35
23	2.87	0.232	0.229	1.310044	11.49	11.34	12.37	12.53
24	3.02	0.236	0.233	1.287554	11.30	11.15	12.80	12.96
25	2.72	0.223	0.221	0.904977	11.44	11.34	12.20	12.31
26	2.84	0.229	0.222	3.153153	11.42	11.07	12.40	12.29
27	2.85	0.231	0.223	3.587444	11.49	11.09	12.34	12.78
28	2.92	0.233	0.231	0.865801	11.41	11.31	12.53	12.64
29	2.75	0.225	0.226	-0.44248	11.46	11.51	12.22	12.17
30	2.94	0.231	0.233	-0.85837	11.26	11.35	12.73	12.62
31	2.55	0.207	0.209	-0.95694	11.09	11.20	12.32	12.20
32	2.77	0.228	0.221	3.167421	11.56	11.20	12.15	12.53
33	2.96	0.234	0.236	-0.84746	11.35	11.45	12.65	12.54
34	2.75	0.221	0.223	-0.89686	11.26	11.36	12.44	12.33
35	2.48	0.202	0.204	-0.98039	11.03	11.13	12.28	12.16
36	3.07	0.251	0.246	2.03252	11.88	11.65	12.23	12.48
37	2.96	0.236	0.235	0.425532	11.45	11.40	12.54	12.60
38	2.73	0.229	0.226	1.327434	11.72	11.57	11.92	12.08
39	2.93	0.234	0.237	-1.26582	11.43	11.57	12.52	12.36
40	2.51	0.201	0.205	-1.95122	10.88	11.10	12.49	12.24
Mean	2.78	0.224	0.223	0.433	11.35	11.30	12.38	12.42
SD	0.16	0.012	0.010	1.566	0.25	0.17	0.23	0.23

*BSA-1, *k-1* and K_m factor-1 were calculated with data from alive animals. BSA-2, k-2 and K_m factor-2 were calculated with data from stripped animals. Deviation of BSA from alive rabbits and stripped rabbits (Deviation (%) = ([BSA_{alive} - $BSA_{stripped}$]/$BSA_{stripped}$) ×100.

2002; Reagan-Shaw et al., 2008). The K_m factor for rabbits weighing 1.8 kg is 12 (*Center for Drug Evaluation and Research, 2002; Reagan-Shaw et al., 2008*). In the present study, average K_m values of 12.38 and 12.44 based on BSA calculation using coating and skinning were obtained, which are consistent with the FDA data. In conclusion, we establish a simple way to calculate rabbit BSA, and provide an accurate Meeh's k constant and K_m values for dose translation between Japanese white rabbits and humans or other animals.

Acknowledgements

This work was partly supported by the National Natural Science Foundation of China (81200207, 81070250), and by the Fundamental Research Funds for the Central Universities (to Liang Bai).

References

Anderson D: Revision of Council of Europe Convention ETS 123 guidelines for the accommodation and care of animals used for experimental and other scientific purposes. Altern. Lab. Anim. 2004, *32(Suppl 1A)*, 183-185.

Breton E, P Choquet, L Bergua, M Barthelmebs, B Haraldsson, JJ Helwig, A Constantinesco & M Fischbach: In vivo peritoneal surface area measurement in rats by micro-computed tomography (microCT). Perit. Dial. Int. 2008, *28*(2), 188-194.

Center for Drug Evaluation and Research CfBEaR. *Estimating the safe starting dose in clinical trials for therapeutics in adult healthy volunteers*. Food and Drug Administration. 2002, Rockville, Maryland, USA, U.S.

Cheung MC, PB Spalding, JC Gutierrez, W Balkan, N Namias, LG Koniaris & TA Zimmers: Body surface area prediction in normal, hypermuscular, and obese mice. J. Surg. Res. 2009, *153(2)*, 326-331.

Crawford JD, ME Terry & GM Rourke: Simplification of drug dosage calculation by application of the surface area principle. Pediatrics. 1950, *5(5)*, 783-790.

Csomos R, G Bosscher, C Mans & R Hardie: Surgical Management of Ear Diseases in Rabbits. Vet. Clin. North. Am. Exot. Anim. Pract. 2016, *19(1)*, 189-204.

Diack SL: The determination of the surface area of the white rat. J. Nutr. 1930, *3(3)*, 289-296.

Fan J, S Kitajima, T Watanabe, J Xu, J Zhang, E Liu & YE Chen: Rabbit models for the study of human atherosclerosis: from pathophysiological mechanisms to translational medicine. Pharmacol. Ther. 2015, *146,* 104-119.

Freireich EJ, EA Gehan, DP Rall, LH Schmidt & HE Skipper: Quantitative comparison of toxicity of anticancer agents in mouse, rat, hamster, dog, monkey, and man. Canc. Chemother. Rep. 1966, *50(4)*, 219-244.

Getz GS & CA Reardon: Animal models of atherosclerosis. Arterioscler. Thromb. Vasc. Biol. 2012, *32(5)*, 1104-1115.

Gibson S & A Numa: The importance of metabolic rate and the folly of body surface area calculations. Anaesthesia. 2003, *58(1)*, 50-55.

Gilpin DA: Calculation of a new Meeh constant and experimental determination of burn size. Burns. 1996, *22(8)*, 607-611.

Gouma E, Y Simos, I Verginadis, E Lykoudis, A Evangelou & S Karkabounas: A simple procedure for estimation of total body surface area and determination of a new value of Meeh's constant in rats. Lab. Anim. 2012, *46(1)*, 40-45.

Kaestner SA & GJ Sewell: Chemotherapy dosing part I: scientific basis for current practice and use of body surface area. Clin. Oncol. (R Coll Radiol). 2007, *19(1)*, 23-37.

Kamaruzaman NA, E Kardia, N Kamaldin, AZ Latahir & BH Yahaya: The rabbit as a model for studying lung disease and stem cell therapy. Biomed. Res. Int. 2013, *2013,* http://dx.doi.org/10.1155/2013/691830.

Kuriyama K, S Fuji, Y Inamoto, K Tajima, T Tanaka, Y Inoue, R Ito, Y Hayashi, A Ito, S Kurosawa, SW Kim, T Yamashita & T Fukuda: Impact of low-dose rabbit anti-thymocyte globulin in unrelated hematopoietic stem cell transplantation. Int. J. Hematol. 2016, *103(4)*, 453-460.

Lee JY, JW Choi & H Kim: Determination of body surface area and formulas to estimate body surface area using the alginate method. J. Physiol. Anthropol. 2008, *27(2)*, 71-82.

Liao J, W Huang & G Liu: Animal models of coronary heart disease. J. Biomed. Res. 2015, *30*, doi:10.7555/JBR.30.20150051

Meeh K: Oberflächenmessungen des menschlichen Körpers. Z. Biol. 1879, *15*, 425-458.

Newcomer CE: The evolution and adoption of standards used by AAALAC. J. Am. Assoc. Lab. Anim. Sci. 2012, *51(3)*, 293-297.

Peng X, JA Knouse & KM Hernon: Rabbit Models for Studying Human Infectious Diseases. Comp. Med. 2015, *65(6)*, 499-507.

Pinkel D: The use of body surface area as a criterion of drug dosage in cancer chemotherapy. Cancer. Res. 1958, *18(7)*, 853-856.

Reagan-Shaw S, M Nihal & N Ahmad: Dose translation from animal to human studies revisited. FASEB J. 2008, *22(3)*, 659-661.

Schein PS, RD Davis, S Carter, J Newman, DR Schein & DP Rall: The evaluation of anticancer drugs in dogs and monkeys for the prediction of qualitative toxicities in man. Clin. Pharmacol. Ther. 1970, *11(1)*, 3-40.

Spector WS (1956). Surface area relationship: mammals In: Spector WS, editor. Handbook of biological data. Philadelphia, Sunders. 1956, *175*.

Vauthey JN, EK Abdalla, DA Doherty, P Gertsch, MJ Fenstermacher, EM Loyer, J Lerut, R Materne, X Wang, A Encarnacion, D Herron, C Mathey, G Ferrari, C Charnsangavej, KA Do & A Denys: Body surface area and body weight predict total liver volume in Western adults. Liver Transpl. 2002, *8(3)*, 233-240.

Wang J & E Hihara: Human body surface area: a theoretical approach. Eur. J. Appl. Physiol. 2004a, *91(4)*, 425-428.

Wang J & E Hihara: A unified formula for calculating body surface area of humans and animals. Eur. J. Appl. Physiol. 2004b, *92(1-2)*, 13-17.

Widdowson EM: How much food does man require? An evaluation of human energy needs. Experientia Suppl. 1983, *44*, 11-25.

Yanni AE: The laboratory rabbit: an animal model of atherosclerosis research. Lab. Anim. 2004, *38(3)*, 246-256.

Zehnder AM, MG Hawkins, EA Trestrail, RW Holt & MS Kent: Calculation of body surface area via computed tomography-guided modeling in domestic rabbits (Oryctolagus cuniculus). Am. J. Vet. Res. 2012, *73(12)*, 1859-1863.

Zernii EY, VE Baksheeva, EN Iomdina, OA Averina, SE Permyakov, PP Philippov, AA Zamyatnin & II Senin: Rabbit models of ocular diseases: new relevance for classical approaches. CNS Neurol. Disord. Drug. Targets. 2016, *15(3)*, 267-91.