## Morphometric Characterisation of an Asian Reference Analytic Morphomics Population (A-RAMP)

# Stewart C. Wang, Chi-Hsun Hsieh, Chi-Tung Cheng, Chien-Hung Chiu, Andrea H. Rossman, Carla Kohoyda-Inglis, Brian Derstine, Sven A. Holcombe, Susumu Ejima, Peng Zhang, Grace L. Su

**Abstract** Previous research has shown that differences in a vehicle occupant's body morphomics (dimensions and composition) predict the type and severity of injuries that occupant sustains in a motor vehicle crash. Data also suggests that the more an occupant varies from standard test surrogates (crash dummies), the greater the crash injury risk. Current test surrogates were developed based on an American population, but the size and stature of the general population varies substantially world-wide. In the current study, our objective was to determine how Asian population morphomics differ from those of an American population. We analysed CT scans from 1,459 live Taiwanese subjects who underwent CT scanning of the chest, abdomen, and pelvis for trauma. Highly automated software was used to precisely measure body dimension and composition in an anatomically indexed manner. Finalised results were compared between the Asian (n=1,459) and US (n=6,479) adult populations. Our detailed morphomic analysis found that Asians differ substantially in many measures of body dimensions and composition from Americans. Since many morphomic measures affect the type and risk of crash injury in motor vehicle crashes, human body finite element models meant to represent specific population segments will be informed by the results of this study.

Keywords computer modelling, human body models, morphomics, population variability, RAMP

#### I. INTRODUCTION

Previous research has shown that differences in a vehicle occupant's body morphomics (dimensions and composition) predict the type and severity of injuries that occupant sustains in a motor vehicle crash (MVC) [1-5]. Data also suggests that the more an occupant varies from standard test surrogates (crash dummies), the greater the crash injury risk [6-8]. Current test surrogates were developed based on a healthy, young American population from six decades ago. While the surrogates have become more sophisticated and now include an entire family, they are still sized up or down from the original American 50<sup>th</sup> percentile male. However, the size and stature of the general population varies substantially world-wide and these crash test surrogates may not accurately predict injuries for those not conforming to the restricted standards.

Simplistically, the body is mainly composed of three types of tissues: bone, muscle, and fat. The bulk of the remainder is composed of visceral organs such as lungs, liver, intestines, etc. With the aging of the general population, decreases in bone mineral density (BMD) and muscle loss with aging (sarcopenia) have increased the number and severity of injuries in MVCs [9,10]. The obesity epidemic was exploding in the United States before showing up in other countries and was initially viewed as a high-income country problem. Across the globe, as food availability increased, obesity rates intensified and have more than doubled since 1980. [11] Data suggest that these population changes have altered injury patterns as well as injury rates.

We previously analysed CT scans from over 6,000 live US subjects to characterise detailed body component size, shape, and composition that allow us to precisely determine population corridors and variability for automotive safety engineers and human body modelers [12]. In the current study, our objective was to determine how Asian population morphomics differ from those of an American population.

S.C. Wang is an Endowed Professor of Surgery in the Department of General Surgery and Director of the Morphomic Analysis Group at the University of Michigan. A. Rossman, C. Kohoyda-Inglis, B. Derstine, S.A. Holcombe, S. Ejima, P Zhang and G.L. Su are affiliated with the International Center for Automotive Medicine at the University of Michigan. H. Chi-Hsun, C. Chi-Tung, and C. Chien- Hung are affiliated with the Chang-Gung Memorial Hospital, Linkou, Taiwan. S.C. Wang, C. Kohoyda-Inglis, and S.A. Holcomb are co-inventors of the analytic morphomics patent. SCW is equity owner of Applied Morphomics, Inc.

#### **II. METHODS**

### **RAMP Study Population**

This study was approved by the University of Michigan Institutional Review Board (HUM00041441). Chest, abdomen, and pelvis CT scans were collected retrospectively from 6,479 patients at the University of Michigan, aged between 16 and 91 years, who were scanned for trauma indications. This population was named the Reference Analytic Morphomics Population (RAMP) version 0.0.5. Age adjusted population distribution curves were generated for both men and women.

## A-RAMP Study Population

A collaboration with the Chang-Gung Memorial Hospital in Linkou, Taiwan, allowed us to retrospectively collect chest, abdomen, and pelvis CT scans from patients older than 16 years of age, who were scanned for trauma and other acute surgical indications. The population of Taiwan is uniquely suited to be considered representative of the greater Asian population as the Japanese ruled the island from 1895-1945. In 1949, large migrations of ethnic Chinese from mainland China arrived. Taiwan is essentially a melting pot of different Asian groups and thus was considered representative. This population was named the Asian Reference Analytic Morphomics Population (A-RAMP) version 1.

## Analytic Morphomics

Analytic Morphomics processing was performed according to methods previously well described [13-15]. All scans were processed semi-automatically using high-throughput image-processing algorithms written in MATLAB 2015a (The MathWorks Inc., Natick, Massachusetts, USA). In brief, we first establish a common coordinate reference system for each scan by identifying individual vertebral levels. Next, we identify the skin and fascial envelopes. Analytic Morphomic measurements are computed from the resulting body composition map. Subcutaneous and visceral fat, pelvis, psoas and dorsal muscle group, as well as spinal trabecular and cortical bone density measurements are then performed at each vertebra level [16]. For this current project, we analysed multiple variables at the level of the third lumbar vertebra (L3); those representative of similarities and differences between the Asian and North American populations are presented below, including:

### Bone

• Bone mineral density (BMD): average voxel radiodensity (Hounsfield units) within a mid-vertebral core sample of trabecular bone.

### Muscle

• Skeletal Muscle area: cross sectional area of the muscle pixels (-29 to 150 HU) between the muscle wall and outer fascial envelope (excluding filled bone, spinal canal and disc).

### Fat

- Total body area: cross sectional area of the body that includes all fat, muscle and bone tissue in addition to visceral organs.
- Subcutaneous fat area: area between the skin and the outer fascial envelope meeting fat density thresholds (-205 to -51 HU).
- Fascia area: total cross-sectional area within the fascial envelope.
- Visceral fat area: area within the fascial envelope meeting fat density thresholds (-205 to -51 HU).

## Statistics

Quantile regression was utilised to depict the relationship between patient age and various analytic morphomics measures for the North American population. We used B-splines with L1 penalties to non-parametrically model the nonlinear trend between age and morphomics, stratified by gender. For each measure, non-crossing quantile curves shown on figures correspond to the 5<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 95<sup>th</sup> percentiles. We then evaluated Asian population in regard to the above North American reference curves, and calculated their

respective percentiles. We used z-scores to quantify the difference between two populations, ARAMP vs RAMP, by comparing calculated Asian percentiles with 50 (the median North American percentile). We also compared the raw values between ARAMP vs RAMP across different age and sex groups using Student's t-test. All statistical analysis was performed using R version 3.2.3. Quantile regression analysis was performed using the R package 'quantregGrowth' [17].

#### **III. RESULTS**

Several selected variables will demonstrate the similarities and differences between the populations. Table I shows the results for measurements of the three most common types of tissue in the body: bone, muscle, and fat [18]. Generally, bone and muscle tissue decreased with aging after 25 years of age, while fat tissue tended to increase until flattening or falling after the sixth or seventh decade; the body location distribution of fat also changed with aging [19].

### TABLE I: BONE, MUSCLE, AND FAT MEASUREMENTS OF A-RAMP COMPARED TO RAMP

Morphomic Variable	Sample Size	Asian population RAMP Percentile Mean	Z-score	P-Value
Bone Mineral Density	1392	47.49	-3.24	0.001
Skeletal Muscle Area	1390	20.156	-55.58	<0.001
Total Body Area	1390	26.183	-39.13	<0.001
Fascia Area	1390	26.602	-30.131	<0.001
Subcutaneous Fat Area	1390	31.342	-31.02	<0.001
Visceral Fat Area	1390	40.08	-14.87	<0.001

Small albeit statistically significant differences in mean BMD for the ARAMP versus RAMP populations were observed. Skeletal muscle area, total body area, fascia area, and subcutaneous fat area were significantly lower in the Asian population when compared to the North American population.

Figures 1 and 2 show the 95<sup>th</sup>, 75<sup>th</sup>, 50<sup>th</sup>, 25<sup>th</sup> and 5<sup>th</sup> percentile curves of the RAMP population, female on the left and male on the right. The ARAMP data are overlaid on the RAMP curves as individual data points. Figure 1 shows a measurement of total body area. Although the Asian data show a broad spread with aging, they average 26<sup>th</sup> percentile of the US population for both males and females. Figure 2 shows that this difference in the raw measure of total body area at L3 was found in both females and males for all three age groups.



Fig. 1. Total Body Area at L3. The 95<sup>th</sup>, 75<sup>th</sup>, 50<sup>th</sup>, 25<sup>th</sup> and 5<sup>th</sup> percentile curves for the North American RAMP population are shown. The Asian RAMP data are overlaid as individual data points.



RAMP v0.0.5 N=4119 ARAMP v1 N=1369

Fig. 2. Total Body Area at L3. Box plots comparing the median and quartile ranges for ARAMP versus RAMP for three adult age groups using Tukey's Honest Significant Difference, p-values are <0.001 for all comparisons among all age groups.

Bone Mineral Density is a snapshot of bone health. Studies have shown that BMD decreases with age in both men and women; this increases the chance of sustaining a fracture in a traumatic event [20-22]. This loss is especially dangerous for women, who lose bone more quickly than men due to hormonal changes as they age. [23] The univariate screening shows L3 trabecular BMD is remarkably similar in both populations. The mean RAMP percentile for the Asian population was 47.49, showing the two populations are highly similar. Figures 3 and 4 show for both males and females that Asian and North American BMD is essentially the same when adjusted for age. There is a general decline in BMD with age in both populations.

Figure 3 also shows two outliers within the graph. Both of these patients suffered vertebral burst fractures

L3 bmdhuvbaligned for age RAMP v0.0.5 with 'ARAMP v1' tag Male Female 750 VB trabecular density @L3 500-250 750 0 ò 10 20 70 80 90 ò 10 50 70 80 90 30 4050 60 20 30 4060 Age (years)

at L3. The software construes the various bone fragments as a solid mass. Therefore, the measurements of these two outliers show a higher density due to the mixing of the trabecular and cortical bone fragments.

Fig. 3. Bone Mineral Density at L3. The 95<sup>th</sup>, 75<sup>th</sup>, 50<sup>th</sup>, 25<sup>th</sup> and 5<sup>th</sup> percentile curves for the North American RAMP population are shown. The Asian RAMP data are overlaid as individual data points.



RAMP v0.0.5 N=4119 ARAMP v1 N=1369

Fig. 4. Bone Mineral Density at L3. Box plots comparing the median and quartile ranges for ARAMP versus RAMP for three adult age groups. Using Tukey's Honest Significant Difference, p-values are <0.001 for all comparisons among all age groups

Muscle tissue area shows an expected peak in the lower age ranges. Young adults have more muscle overall, as well as denser muscles (showing very little fatty infiltration). The RAMP curves in Figure 5 show this is the case with a maximum reached during early adulthood followed by a gradual decline as the population ages. The average Asian population is at approximately the 20<sup>th</sup> percentile of the North American (RAMP) population in total muscle area for both males and females. Figure 6 shows substantial differences in the median muscle area at L3 between the Asian and North American populations for males and for females in all three adult age groups.



Fig. 5. Skeletal Muscle Area at L3. The 95th, 75th, 50th, 25th and 5th percentile curves for the North

American RAMP population are shown. The Asian RAMP data are overlaid as individual data points.



RAMP v0.0.5 N=4086 ARAMP v1 N=1369

Fig. 6. Skeletal Muscle Area at L3. Box plots comparing the median and quartile ranges for ARAMP versus RAMP for 3 adult age groups. Using Tukey's Honest Significant Difference, p-values are <0.001 for all comparisons among all age groups.

Subcutaneous fat is the fat located between the skin and the outside of the fascial envelope. Figure 7 shows the curves for the RAMP population, which demonstrate that the greatest concentration of subcutaneous fat is in the younger age groups. Again, the Asian population is concentrated mostly in the lower areas of the RAMP percentile curves (ARAMP mean = 31st percentile). Figure 8 shows that in all three age groups and for both males and females, the North American population had substantially more subcutaneous fat than the Asian population.

#### 375



Fig. 7. Subcutaneous Fat Area at L3. The 95th, 75th, 50th, 25th and 5th percentile curves for the North American RAMP population are shown. The Asian RAMP data are overlaid as individual data points.



RAMP v0.0.5 N=4119 ARAMP v1 N=1369

Fig. 8. Subcutaneous Fat Area at L3. Box plots comparing the median and quartile ranges for ARAMP versus RAMP for three adult age groups. Using Tukey's Honest Significant Difference, p-values are <0.001 for all comparisons among all age groups.

Visceral fat is the fat located around the internal organs inside the fascial envelope and tends to increase as people age. Figures 9 and 10 show that the relatively low visceral fat area in the young RAMP population increases dramatically with age. The Asian population appears to have similar amounts of visceral fat as their North American counterparts during young adulthood. However, with advancing age the North American population begins to accumulate substantially more visceral fat, especially in males.



Fig. 9. Visceral Fat Area at L3. The 95th, 75th, 50th, 25th and 5th percentile curves for the North American RAMP population are shown. The Asian RAMP data are overlaid as individual data points.



RAMP v0.0.5 N=4119 ARAMP v1 N=1369

Fig. 10. Visceral Fat Area at L3. Box plots comparing the median and quartile ranges for ARAMP versus RAMP for three adult age groups. Using Tukey's Honest Significant Difference, p-values are <0.001 for all comparisons among all age groups.

## **IV.** DISCUSSION

According to the US National Center for Health Statistics, obesity frequency is 39.8% among adults in the US. Among non-Hispanic whites, that number is 37.9%, while Asian Americans' incidence of obesity is 12.7% [24]. The standard to measure obesity is body mass index (BMI >30 kg/m2). Our data, the first to directly compare the morphomics of large North American and Asian populations, are broadly consistent with those observed in the US ethnic groups. Our current results demonstrate that our North American and Asian (Taiwanese) trauma patient samples differ in specific ways, namely, in distributions of the quantity of fat and muscle of their "typical"

population. While bone density differed little, Asian muscle area and fat area distributions were generally much smaller than the North American reference. North American crash test dummy outer dimensions and/or mass distribution may therefore poorly approximate Asian vehicle occupants. Region-specific dummies and human body models may need to be developed to optimally protect occupants of vehicles designed for specific world markets.

Our group has published extensively on the effect of body composition on injury severity during motor vehicle crashes. Zhang *et al* first investigated anatomical morphomic variables to predict thoracic injury in frontal impacts using a model-averaged logistic regression approach [25]. That study showed that chest eccentricity (highly correlated with fascia area), BMD, and spine alignment were highly associated with chest injury. Parenteau *et al* [26] also showed that BMD and visceral fat area were significantly associated with abdominal injury. The importance of these morphomics was also shown in predicting lower-extremity injury (Wang *et al*). We have also shown that heterogeneity in vertebral column angles, torso depth, H-point location, and subcutaneous fat area in the back. These variables could impact an occupant's seating position and, in turn, affect their injury risks. All in all, we have shown that morphomics play a key role in evaluating injuryrisk and better dummy and computer modeling. However, the majority of these studies were based entirely on the North American population. The major contribution of this study is to highlight the body composition differences among different populations around the world. Some of the Asian morphomics differ greatly, e.g. fascia area is at only 25<sup>th</sup> percentile compared to a North American population, and we know morphomics are crucial in predicting injury risk. This calls for more comprehensive research to understand this heterogeneity and its impact, which may lead to better and safer cars.

The use of Taiwanese subjects to represent the Asian population could be problematic. However, due to the desirability of controlling the land mass, many groups have invaded this area over the course of centuries. For instance, the Japanese controlled the island from 1895-1949. In addition, many ethnic Chinese came to Taiwan from mainland China after 1949. We believe this mixing of the population provides us with the foundation to use these subjects as representative.

The US RAMP population represents approximately 6,000 University of Michigan patients who were scanned for traumatic indications. This population has allowed us to compare patients across sex and age to develop corridors illustrating an "average" person.

#### V. CONCLUSIONS

Asians differ substantially in many measures of body dimensions and composition from North Americans according to our detailed morphomic analysis. Since many morphomic measures affect the type and risk of crash injury in motor vehicle crashes, human body finite element models and anthropomorphic test devices meant to represent specific population segments will be informed by the results of this study.

#### **VI.** ACKNOWLEDGEMENTS

The authors are grateful for the technical assistance of Brian Ross, Nidhi Shah, and June Sullivan in the morphomic processing and inspection of medical imaging scans.

#### **VII. REFERENCES**

- Ejima, S., Holcombe, S.A., et al. The Effect of Rib Fracture Pattern in the Obese. Proceedings of 2017 IRCOBI Conference, 2017. Antwerp, Belgium.
- [2] Ejima, S., Kohoyda-Inglis, C., et al. Lower Extremity Fracture in Patients with Obesity in Real-World Crash Data. Proceedings of 25th International Technical Conference on the Enhanced Safety of Vehicles, 2017. Detroit, MI
- [3] Holcombe, S.A., Ejima, S., et al. Patterns of local and regional variation in ribcage anatomy, in *Japan Society of Automotive Engineers*. 2009, JSAE: Yokohama, Japan.
- [4] Holcombe, S.A., Ejima, S., Huhdanpaa, H., and Wang, S.C. Ribcage characterization for FE using finite element CT processing, in *Japan Society of Automotive Engineers*. 2008, JSAE.

- [5] Holcombe, S.A., Ejima, S., and Wang, S.C. Calcification of Costal Cartilage in the Adult Rib Cage. *Proceedings of 2017 IRCOBI Conference*, 2017. Antwerp, Belgium
- [6] Jones, M.L.H., Ebert, S.M., Hu, J., and Reed, M.P. Effects of High Levels of Obesity on Lap and Shoulder Belt Paths, in 2017 IRCOBI Conference 2017, IRCOBI: Antwerp, Belgium.
- [7] Hu, J., Zhang, K., et al. Stature and Body Shape Effects on Driver Injury Risks in Frontal Crashes: A Parametric Human Modelling Study, in 2017 IRCOBI Conference. 2017, IRCOBI: Antwerp, Belgium.
- [8] Wang, S.C. Treat the Patient, Not Just Their Disease, in 2017 IRCOBI Conference. 2017, IRCOBI: Antwerp, Belgium.
- [9] Malekpour, M., Bridgham, K., et al. The Effect of Sarcopenia on Outcomes in Geriatric Blunt Trauma. Am Surg, 2017.
  83(11): p. 1203-1208
- [10] Steihaug, O.M., Gjesdal, C.G., et al. Sarcopenia in patients with hip fracture: A multicenter cross-sectional study. PLoS One, 2017. 12(9): p. e0184780
- [11] Overweight and Obesity Fact Sheet, S.D.a.H. Environments, Editor. 2011, World Health Organization: Regional Office for South-East Asia.
- [12] Wang, S.C. Growing Obesity: Concerning Implications for the Burden from Crash Injury. *Proceedings of the Japan* Society of Automotive Engineers 60th Annual Meeting, 2007
- [13] Parenteau, C., Holcombe, S.A., Zhang, P., Kohoyda-Inglis, C.J., and Wang, S.C. The Effect of Age on Fat and Bone Properties along the Vertebral Spine. SAE International Journal of Transportation Safety, 2013. 122(9): p. 15
- [14] Englesbe, M.J., Patel, S.P., et al. Sarcopenia and mortality after liver transplantation. J Am Coll Surg, 2010. 211(2): p. 271-8
- [15] Lee, J.S., He, K., et al. Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair. J Vasc Surg, 2011. 53(4): p. 912-7
- [16] Morphomics Analysis Group. "Data Dictionary" Internet http://www.med.umich.edu/surgery/morphomics/data\_dictionary.html. [cited 2019 May 1].
- [17] Muggeo, V.M.R., Sciandra, M., Tomasello, A., and Calvo, S. Estimating growth charts via nonparametric quantile regression: a practical framework with application in ecology. *Environmental and Ecological Statistics*, 2013. 20: p. 12
- [18] Morphomics Analysis Group. "Morphomics" Internet http://www.med.umich.edu/surgery/morphomics/index.html. [cited 2019 5/1/2019].
- [19] Holcombe, S.A. and Wang, S.C. Subcutaneous Fat Distribution in the Human Torso. *Proceedings of International Research Council on the Biomechanics of Injury (IRCOBI)*, 2014. Berlin, Germany
- [20] Cummings, S.R., Black, D.M., et al. Appendicular bone density and age predict hip fracture in women. The Study of Osteoporotic Fractures Research Group. *JAMA*, 1990. 263(5): p. 665-8
- [21] Mikula, A.L., Hetzel, S.J., Binkley, N., and Anderson, P.A. Validity of height loss as a predictor for prevalent vertebral fractures, low bone mineral density, and vitamin D deficiency. Osteoporos Int, 2017. 28(5): p. 1659-1665
- [22] Schuit, S.C., van der Klift, M., et al. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. *Bone*, 2004. 34(1): p. 195-202
- [23] Nih Consensus Development Panel on Osteoporosis Prevention, D. and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA, 2001. 285(6): p. 785-95
- [24] Hales, C.M., Carroll, M.D., Fryar, C.D., and Ogden, C.L. Prevalence of Obesity Among Adults and Youth: United States, 2015-2016, N.C.f.H. Statistics, Editor. 2017, US Department of Health and Human Services: Hyattsville, Maryland. p. 8.
- [25] Zhang, P., Parenteau, C., et al. Prediction of thoracic injury severity in frontal impacts by selected anatomical morphomic variables through model-averaged logistic regression approach. Accid Anal Prev, 2013. 60: p. 172-80
- [26] Parenteau, C.S., Zhang, P., Holcombe, S., Kohoyda-Inglis, C., and Wang, S.C. Can anatomical morphomic variables help predict abdominal injury rates in frontal vehicle crashes? *Traffic Inj Prev*, 2014. 15(6): p. 619-26