Keynote Lecture

Treat the Patient, Not Just Their Disease

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INTRODUCTION

Around the world, road injury is the tenth leading cause of death, killing 1.3 million in 2015 alone. [1] In addition, 20-50 million people are injured in motor vehicle crashes worldwide. [2] These incidences are estimated to cost $518 billion globally. [3]

In the early days of automotive safety development, it was relatively easy to determine how occupants were injured. Vehicles were made mostly of metal with sharp edges, stiff interior panels, and great expanses of glass. In a crash, occupants were flung around, striking these vehicle structures with often lethal results – steering wheels in the chest, heads through windshields, and extremities flailing. Improvements in passive automotive safety, such as seatbelts, air bags, and friendly interior surfaces, have ushered in a steady but slow decline in morbidity and mortality. Furthermore, with active safety systems such as forward collision warnings, electronic stability, and speed assist becoming more prevalent in the fleet, these numbers will continue to drop, albeit slowly. Such vehicle-centric improvements have saved numerous lives and decreased the number of those living with debilitating injuries; however, occupants continue to be injured and killed in large numbers. The trajectory of safety improvements overall is flattening and stands at odds with the global vision to eliminate deaths due to vehicle crashes. To achieve Vision Zero [4], it will be necessary to change the paradigms that have guided safety efforts thus far. [5]

Current paradigms for vehicle safety development have depended on evaluations based largely on well-controlled tests utilizing standardized occupants calibrated carefully to respond the same way each time – physical anthropomorphic test devices (ATDs/crash dummies) or virtual human models that are meant to represent the population at large. Unfortunately, the real-world population has changed substantially in the decades since these test devices were first developed. In addition to changing, the population has also become far more diverse and therefore more variable.

Obesity

Once the problem of only a few wealthy nations, obesity has become a rising problem worldwide. According to the WHO, obesity has more than doubled since 1980. Across the globe, 15% of women and 11% of men age 18+ were obese according to the 2014 Global Health Observatory data. (Figure 1) [6] Along with suffering from a host of co-morbidities (diabetes, cardiovascular disease, stroke, and hypertension) [7], the obese are not being protected in vehicles the same way their leaner counterparts are. For instance, seat belts have been tuned to optimally fit the average-sized occupant. For an obese occupant, the belt may not be comfortable or may not fit around them completely. This can lead to the occupant using an aftermarket belt extender which distorts the position of the belt, ultimately leading to misuse, or not to wear a seatbelt at all.

In early International Center for Automotive Medicine (ICAM) research, we determined occupants carrying extra weight were not as likely to suffer head injuries. [8,9] This benefit, however, was overwhelmed by the number and severity of lower extremity injuries sustained by overweight and obese occupants. [10-12] These injuries have long term effects on the mobility and functional outcome for non-obese occupants. In the obese population, lower extremity injuries can be a death sentence. [13,14]

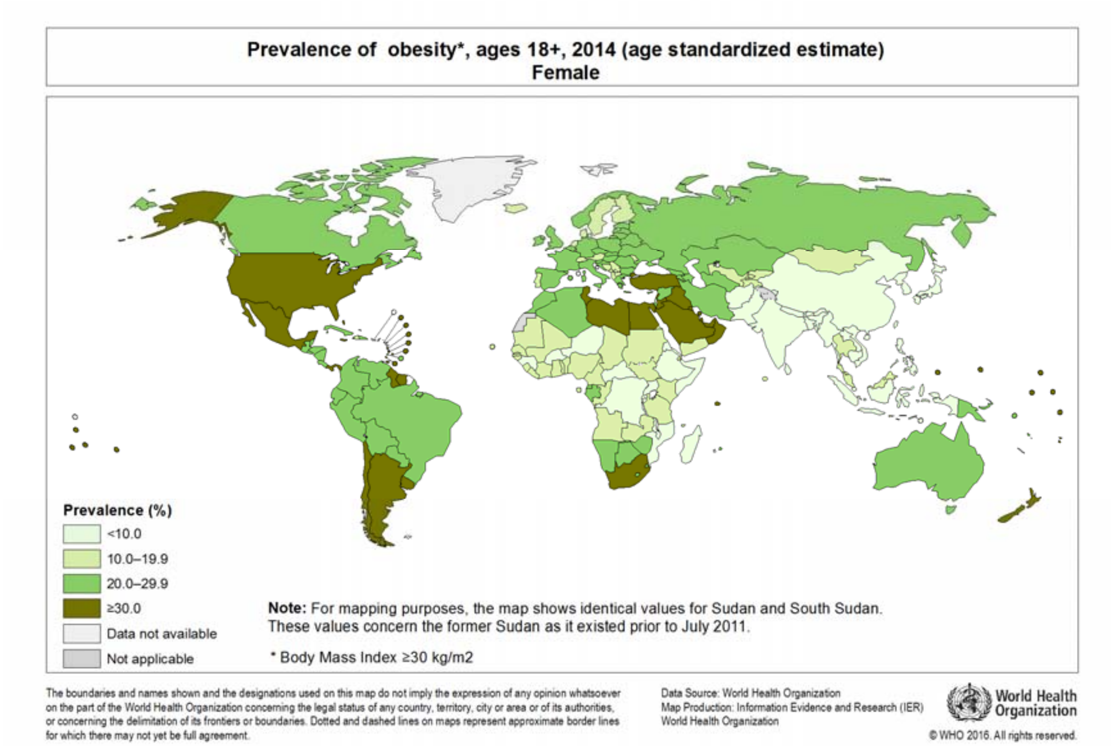

Figure 1 Female Obesity Worldwide

Aging

The overall population is also aging as life expectancy has improved worldwide. (Figure 2) [15] Because injury is the leading cause of death in the US from birth through age 44 and it is more common for older people to die from heart disease or cancer, trauma is often thought to be a disease that afflicts the young. In fact, elderly motor vehicular trauma is a large and growing problem as the general population ages and continues to drive. [16] Licensing rates for drivers over age 65 have increased, as have the number of trips driven and the length of those trips. [17] Not only are current seniors are more mobile than any previous generation, they experience a disproportionately higher crash involvement rate. [18] Elderly drivers have more crashes per million vehicle miles traveled than any other age group except for the youngest, most inexperienced drivers

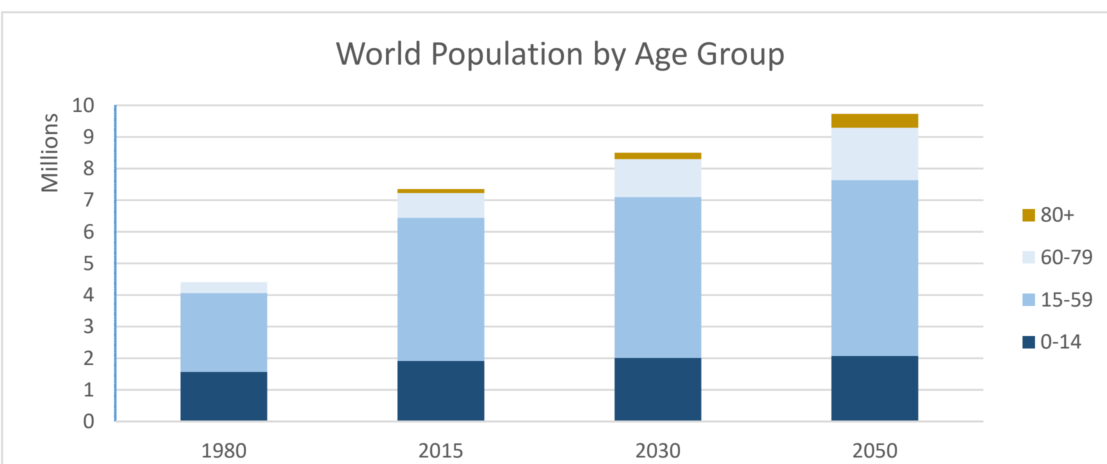

Figure 2 Increase in the elderly from 1980-2050

from 16-25. [19,20] Side impact collisions, most common at intersections, are particularly serious to older drivers in terms of injury and fatality potential. [21,22]

The Insurance Institute for Highway Safety (IIHS) has reported that drivers over 74 were involved in more fatal crashes per 100,000 licensed drivers than any other age group over 30. [23] Several studies have reported that increased injury severity score (ISS) predicted a worse outcome and for any given score, the elderly did poorly compared to a similar cohort of younger occupants. [24-26] This age-dependent survival decrement has been noted for all mechanisms of injury, all body regions, and all ISS. Given equivalent injury scores, the over-65 age group also has higher admission rates, longer hospital lengths of stay, and higher mortality rates than younger patients. The rate of recovery for the older age group is much slower, and they require nearly double the number of outpatient visits post-operatively [27] and many never regain their prior level of health.

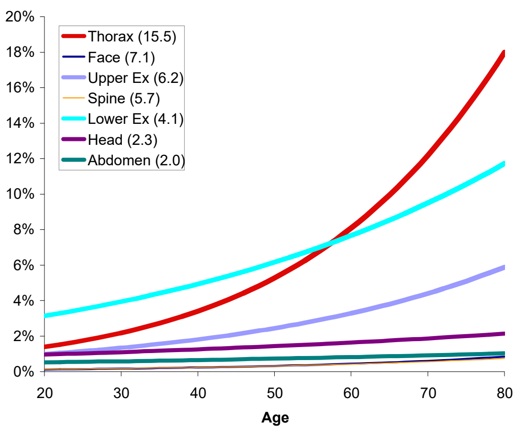

Figure 3 Injury risk by body region v. age

Increased vulnerability of the elderly is particularly concerning as current crash studies suggest that older people are not benefitting from the latest generation of vehicle safety systems as much as the younger adult population. This disparity may widen further as the vehicle fleet modernizes, adopting the newest generations of vehicle safety systems optimized for younger occupants. While chest injuries have decreased for young occupants, the elderly still suffer from major thoracic harm such as aortic injuries, rib and sternal fractures, and pneumo/hemothoraces – even in minor severity crashes. [28-31] ICAM analyzed the National Automotive Sampling System (NASS) database to determine the effect of age on injury risk to different body regions. Figure 3 shows the injury risk versus age for belted drivers involved in frontal crashes with severity of 30 MPH. It is evident that the chest is particularly vulnerable to crash injury as the subject ages, more so than other body regions.

These challenges facing vehicle safety professionals are analogous to those facing medical professionals like myself trying to improve the health of the same population, which is changing and becoming ever more variable. We cannot choose or design the people who need medical treatment, just as we cannot choose the people allowed to travel in vehicles. In medicine, we have strived to address population changes and variability by studying the effects of patient differences on clinical outcomes and individualizing their treatments to achieve a more optimal outcome that that from generic approaches. The development and utilization of biochemical, genetic, and other biomarkers has led to improved patient outcomes. Simplified, we are starting to treat each patient individually, not just their disease as we used to when we did not appreciate or understand the effect of differences within the population. Rather than treating variability as an obstacle, precision medicine is trying to use it as an opportunity to better understand and treat patients. (Figure 4)

I have 30 years' experience as a trauma surgeon who sees and treats the real world injuries resulting from MVCs. Over the past twenty years, I have also had the opportunity to collaboratively analyze crashes with biomechanics and automotive engineers. Having also trained as a basic scientist, I tried to distill our joint research into a paradigm capable of framing observations and generating hypotheses that could be tested to understand the underlying causation mechanisms. Given my medical background, my perspective is highly biased toward that of the person/patient/occupant.

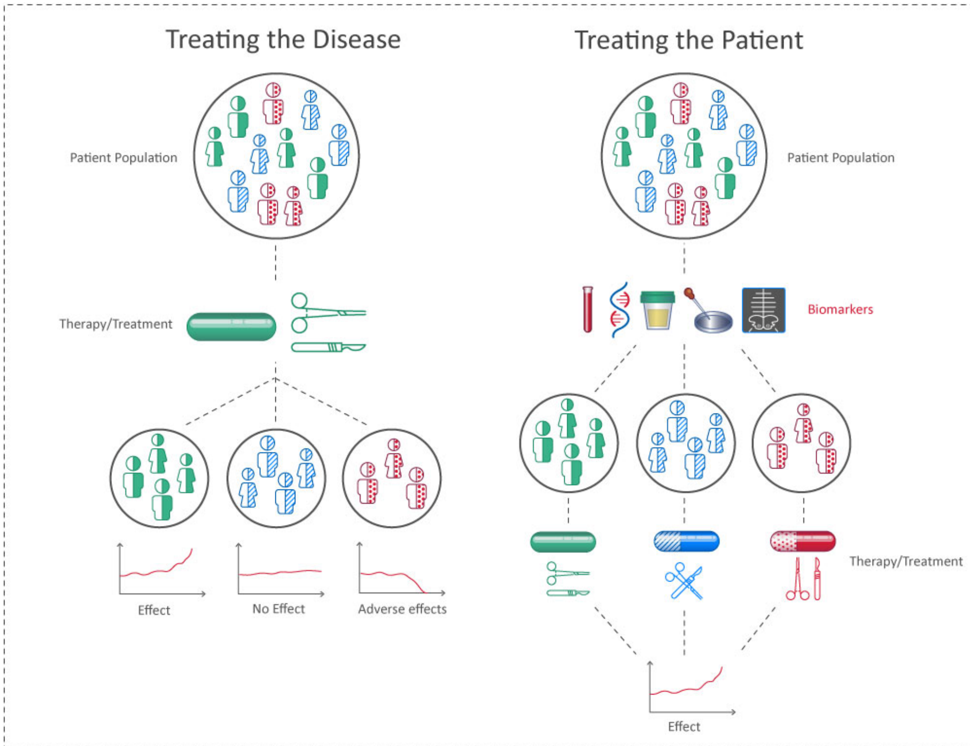

Figure 4 Personalized Medicine

Within my paradigm:

- People are highly variable and change constantly: people cannot be engineered
- The whole population must be protected, not just idealized population segments or idealized surrogates
- Injuries are the result of tissues failing locally under excessive force concentrations
- The severity of insult forces combined with the geometry and condition of the tissues being acted upon are the key determinants of whether injury occurs
- Objective, granular and quantitative measures of occupant geometry and condition are necessary to describe people to automotive engineers

While it is impossible to regulate or engineer the size and shape of an occupant, there are observable trends in body habitus that can be used to improve safety for everyone. Relatively little is known about the specific physical factors that contribute to high-energy injury tolerance in live human subjects. Previous attempts to employ anatomic data from computed tomography (CT) scans have used a few select data sets from uninjured individuals chosen for their approximation of a target stature to create idealized virtual models. [32,33] We instead took the divergent approach of studying a much larger population to establish the distribution of important body composition parameters within the entire adult trauma population. Through this laborious but fundamental process, it became possible to understand how and why body differences alter injury tolerance.

As medically-based researchers, our research team's need to provide good data to automotive engineering collaborators in their quest to better understand and prevent crash injuries required us to develop new analytic techniques. Despite being subjected to similar crash events, individuals sustain widely different injuries as a result of variations in size and condition of their bodies. "Young" or "old", "male" or "female" were insufficiently granular descriptors of body characteristics to permit analysis of age or gender's effect on crash injury mechanisms and risk. Our engineering collaborators needed a finer and, most importantly, a more quantitative method of assessing body geometry and tissue characteristics. To facilitate analysis across a large, variable population and index anatomical measurements and locations in 3D space, we developed customized software that allows raw, archival CT data to be processed into measurements of anatomic structures with defined geometry and tissue properties – a process called analytic morphomics. Each morphomic element is captured precisely using algorithms and definitions that ensure consistent measurements stored in a spatial database. Bony structures are the scaffold for the body and provide excellent landmarks for soft tissues; they are also relatively easy to segment away from other body structures. Thus, the morphomic analysis process begins with segmentation, visual identification, and tagging of bony anatomic landmarks. Using the spatial location of these landmarks as reference, the process segments out soft tissues and visceral organs via custom semi-automated image processing algorithms. The locations of these segmented soft-tissue structures are entered into a relational database. The stored locations of bony landmarks are used to pull the surrounding volume of CT scan data for more detailed image analysis. This ability to load and analyze only the volume of interest markedly improves computational efficiency.

The use of CT scans performed on crash occupants has several advantages. CTs are done in the initial evaluation of crash victims, before medical treatment (fluids, blood, surgery, stress, and metabolism) have a chance to alter the body geometry and composition. While some body factors can be altered by injuries, the body's symmetry as well as the fact that most portions of the body are not injured, allows morphomics to provide an excellent assessment of an individual's baseline condition before the crash. CTs are stored in pristine shape and are unchanged by the passage of time, facilitating analysis once other important data have been collected. Additionally, CTs are digital files that can be analyzed and reanalyzed in a non-destructive manner.

How do morphomic differences affect injury outcome?

A major population trend is the large and sustained increase in the number of elderly people. Multiple studies have reported that the elderly are far more susceptible to chest injuries and fare more poorly from a clinical perspective as a result of those chest injuries compared to the young. Recent changes to the vehicle structure as well as the addition of lateral torso and curtain airbags appear to be reducing injury risk and severity in side impact crashes. [34,35]

However, side impact crashes are more dangerous for a given crash severity than frontal crashes or rear-end crashes. [36,37] As chest injuries in particular are frequently observed, we examined the side-impact crash cases that we have collected at ICAM over the past two decades. Our case collection process is based on the Crash Injury Research and Engineering Network (CIREN), in which we participated for 13 years, with a NASS-CDS type vehicle assessment as well as detailed medical data collection. ICAM cases go substantially beyond CIREN by adding much more detailed medical data collection including anatomic injury mapping as well as morphomic data regarding the crash occupant's body geometry and condition.

The subset of ICAM case data utilized for this analysis included: principal direction of force (PDOF), seatbelt use, intrusion measures, and crash severity (as determined by WINSMASH or EDR download). The occupant demographic data included: age, gender, height, weight, and BMI. The occupant morphomic factors included: regional body size, composition, and geometry (skeletal, muscle, fat, overall). We had over 500 morphomic measures available for analysis and began by performing a univariate screening of the factors that were associated with MAIS2+ injuries to the chest region (4T). Due to the fact that many of the morphomic variables were not normally distributed, various statistical techniques were used to investigate the differences in morphomic variables between injured vs non-injured groups, including t-test, Wilcoxon signed-rank, and median test.

Table 1 shows results from the Wilcoxon test since it is robust for non-normally distributed variables as in many of morphomic variables. The most significant morphomic variables associated with MAIS2+ chest injuries were related to body shape. These include SP2BACKSKIN or the depth of subcutaneous fat from the spinous process to the posterior skin; body depth, the distance from the front of the vertebral body to the anterior skin midline; and total body cross sectional area at different vertebral levels. Multiple vehicle crash factors were significant including the total count of intrusions as well as the extent of lateral intrusion (upper, mid, and total). The appearance of lateral intrusions high in the screening provides context, as lateral intrusions are accepted to be ground truth for increased chest injury risk based on other studies such as NASS. The appearance of the same morphomic factor at multiple vertebral levels as well as the appearance of variables of a similar class (body shape) coupled with the absence of many other classes of variables make it less likely that these observations were purely due to chance. It is interesting to note that morphomic variables were as significant as intrusion and more significant than age.

We next performed multivariate analysis to confirm the importance of the different classes of variables (vehicle, demographic and morphomic) for the prediction of MAIS2+ chest injury in side impact crashes. As we had data for the same morphomic measure at multiple vertebral levels, we selected values from one vertebral level only for inclusion in the model. We also selected morphomic variables to represent all the major body tissues (bone size, bone quality, muscle size, muscle quality, etc.) for inclusion in multivariate analysis.

	Statistic	P-value
SP2BACKSKIN.T5	3.357	0.00079
SP2BACKSKIN.T6	3.300	0.00097
INTR.TOTAL.LAT	-3.047	0.0023
BODYDEPTH.T4	2.972	0.0030
BODYDEPTH.T3	2.949	0.0032
BODYDEPTH.T5	2.894	0.0038
BODYDEPTH.T6	2.861	0.0042
SP2BACKSKIN.T4	2.806	0.0050
INTR.COUNT	-2.794	0.0052
INTR.UPP.LAT	-2.780	0.0054
VB2FRONTSKIN.T6	2.727	0.0064
VB2FRONTSKIN.T3	2.679	0.0074
SP2BACKSKIN.T7	2.667	0.0077
BODYDEPTH.T2	2.637	0.0084
VB2FRONTSKIN.T5	2.597	0.0094
INTR.MID.LAT	-2.550	0.01
VB2FASCIA.L5	-2.549	0.01
TOTALBODYAREA.T3	2.506	0.01
TOTALBODYAREA.T4	2.491	0.01
VB2FRONTSKIN.T4	2.472	0.01
TOTALBODYAREA.T6	2.440	0.01
TOTALBODYAREA.T2	2.436	0.01
TOTALBODYAREA.T5	2.435	0.01
DELTA-V	-2.043	0.04
AGE	-1.076	0.28

Table 1 Univariate Analysis of Morphomic Variables Associated with MAIS2+ Chest Injuries in Side Impact Crashes

Logistic regression models were fitted using crash, demographic, and morphomic variables for occupants with and without MAIS2+ chest injury. A similar methodology was previously described in Burnham and Anderson [38] and Zhang et al. [39] We utilized a model-averaging methodology that predicted crash injury risk using vehicle, demographic, and morphomic variables to assess the importance of individual predictors. Logistic regression models were fitted using all possible configurations of vehicle, demographic, and morphomic variables, and models were ranked by the Akaike Information Criteria (AIC). The final predictive results were developed using this approach, based on the top 100 models in the AIC ranking. Model-averaging minimized model uncertainty, decreased the overall prediction variance, and provided an approach to evaluating the importance of individual variables. There were 12 variables investigated: four vehicle, three demographic, and five morphomic. More than 4,000 logistic models were investigated in total. The models were characterized into four scenarios to assess individual variable contribution to injury risk:

1. Vehicle/crash variables
2. Vehicle/crash + demographic variables
3. Vehicle/crash + morphomic variables
4. Vehicle/crash + demographic + morphomic variables

The AIC and the area under the receiver operating characteristic curve (AUC) were reported in each model. The models were re-fitted after removing each variable one at a time. The increases of AIC and the decreases of AUC were then assessed to measure the contribution and importance of the individual variables in each model. The importance of the individual variables was also determined by their weighted frequencies of appearance in the top 100 selected models. This approach is helpful when addressing variable selection, building prediction models, and assessing the importance of different variables. The variables and models were selected to produce top models with the most robust predictions. The final predictive results were developed using this approach, based on the top 100 models according to the AIC ranking.

The prediction performance of optimal regression models was assessed using the receiver operating characteristic (ROC). ROC plots the model sensitivity as a function of specificity. Models were then compared using the area under the curve (AUC). Using vehicle variables alone in the injury prediction model (Simple Model), the AUC was 0.652. With the addition of demographic factors, the AUC improved to 0.742. When morphomic variables were added to the vehicle variables, the AUC improved to an excellent 0.798. When all three types of variables (vehicle, demographic, and morphomic – Full Model) were included in the injury prediction model, the AUC was 0.835. (Figure 5) The large jump in AUC between the models with morphomics compared to those without morphomics highlights the importance of morphomic variables in whether individuals sustain thoracic injuries in side impact motor vehicle crashes. Examination of the variables included in the final model supports the conclusion that soft tissue quality, especially that of the muscles – which can become infiltrated by fat with aging, obesity, or deconditioning – contributes substantially to chest injury risk in lateral MVCs.

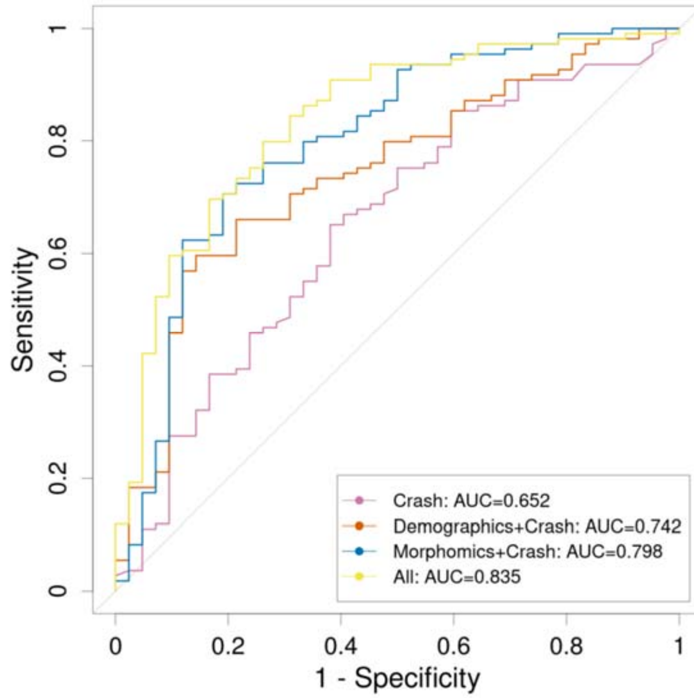

Figure 5 Prediction Performance of Models Using Vehicle, Demographic, and Morphomic Variables for MAIS2+ Chest Injuries in Side Impacts

In the above analysis, we included morphomic factors that were global from a body perspective (size, depth, aspect ratio) as well as those related to different tissues and organ systems (bone mineral density, bone thickness, muscle density, muscle cross sectional area, fat cross sectional area). We have also found that morphomic variables at the anatomic component level (rib angles, bone thickness variability, rib curvature, etc.) are important predictors of specific anatomic injuries.

Having found that different morphomic factors are predictive of injury outcome, we next set out to determine the population context of these factors. What is the variability and distribution of those morphomic factors in the population at risk and how do they relate to age and gender (risk factors that have previously been characterized)?

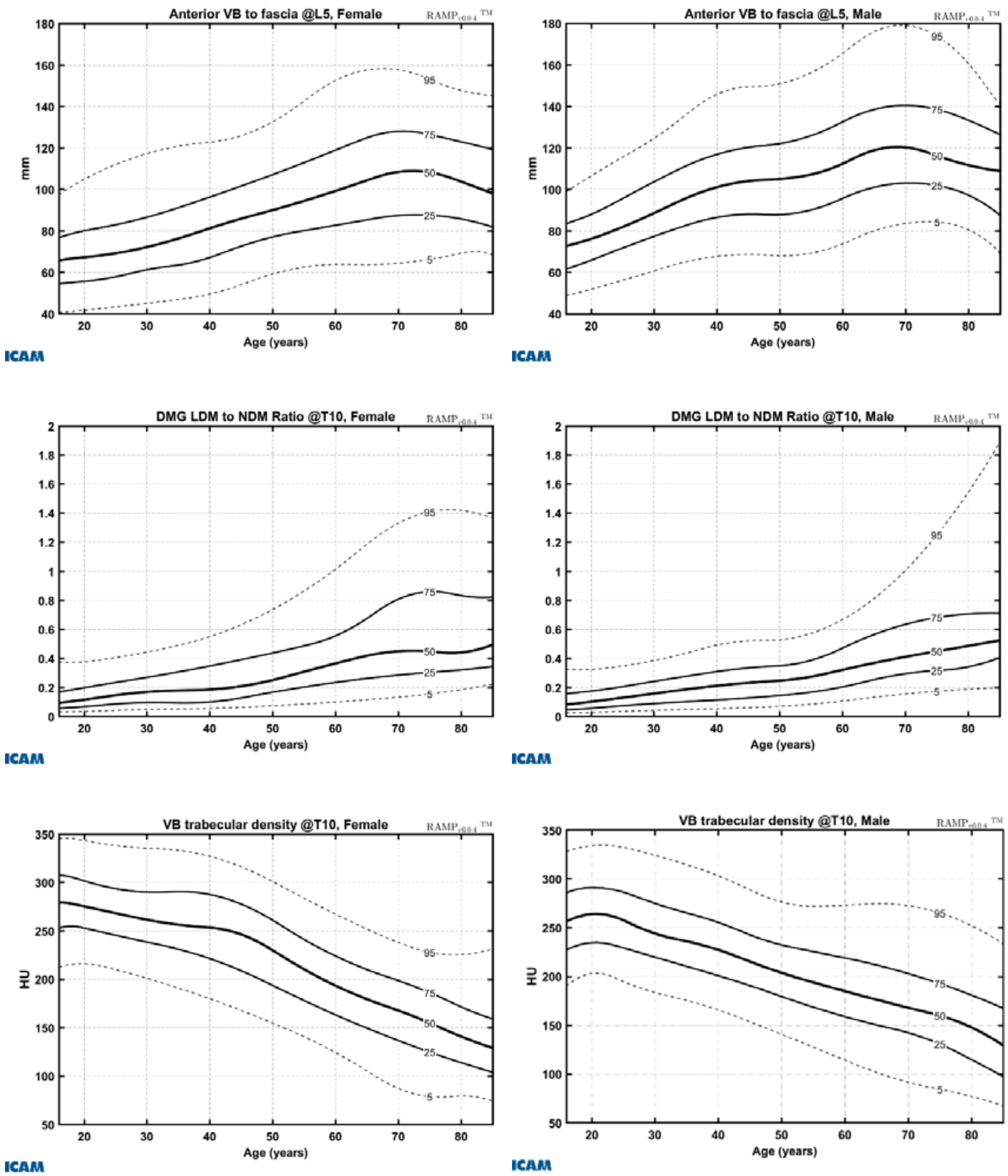

Figure 6 RAMP Charts for Morphomic Variables Predictive of Chest Injury in Side Impact Crashes

CT scanning exposes patients to ionizing radiation and is nearly always done for a medical indication. As such, most available CT scans are done in patients with an active disease process, such as cancer, which may alter their body composition. The population closest to being representative of the general population is the trauma population. Trauma affects individuals of all ages and CT scans are done as part of the standard evaluation of patients who have experienced blunt trauma. This trauma population contains patients who have no significant prior medical history as well as others with multiple medical conditions. We therefore performed morphomic analysis on a population of 6,000 trauma patients scanned as part of their initial evaluation at the University of Michigan. Figure 6 summarizes the distribution of the morphomic factors identified to be significant for MAIS2+ chest injuries within this population, which we have named the Reference Analytic Morphomics Population (RAMP). [40] The figures are separated by gender and show the effect of age on the distribution and variability of each morphomic factor.

Knowing that a certain factor affects a body's risk as well as its variability in the general population provides motivation to examine whether countermeasures can be developed to better mitigate those injuries, but additional detail is needed to provide context for those engineering and design efforts. We therefore sought to obtain an estimate of the injury risk effects of that variation. For each morphomic variable, logistic regression was used to estimate the odds of MAIS 2+ chest injury. Confounding variables including Delta V, belt status, and gender were also controlled for in the logistic model. Odds ratios and risk ratios were calculated between 25th and 75th percentiles, 10th and 90th, 5th and 95th, and 1st and 99th of the morphomic variable for a belted male in a 20 mph crash-severity lateral crash. Figure 7: Effect of Vertebra to Fascia, Muscle Density Ratio, and Trabecular Bone Density on chest injury risk for a 20 MPH SIDE IMPACT, Male, Belted and estimate the effect of differences in a single body factor on MAIS2+ chest injury risk. The figures highlight the differences in risk between a morphomically-50th percentile male and those at 1st, 5th, 10th, 25th, 75th, 90th and 95th, and 99th percentile.

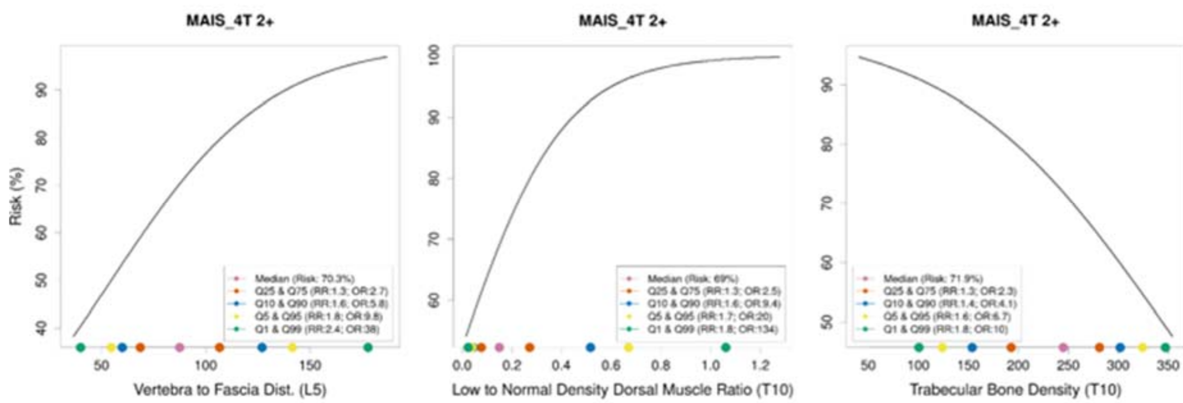

Figure 7: Effect of Vertebra to Fascia, Muscle Density Ratio, and Trabecular Bone Density on chest injury risk for a 20 MPH SIDE IMPACT, Male, Belted

These risk curves were estimated based on the logistic regression and additive model. Hence, we assume that the effect of factors on odds of injury has a linear relationship. We only adjust for Delta-V, belt status, and sex. The observational nature of this research will not allow us to draw causal interpretations. Nonetheless, we believe that such data can inform parametric testing of human body finite element models (FEMs), as morphomics provide more tangible understanding of the human body than age and BMI. Such testing will provide some insight into how variability in particular morphomic features affects the biomechanical mechanisms of injury.

FEMs are playing an increasingly prominent role in vehicle safety design and development. [41-43] Our morphomics data can provide the input data required for such models including geometry and material properties (through radiologic imaging surrogate values such as bone mineral density). One additional need for human body FEMs is injury frequency mapping. FEMs generate stress-strain maps of the human body. Joint analysis of FEM results with injury frequency maps from live crash subjects can provide partial validation and guide the future development of these models. Figure 9 shows rib fracture frequency maps for crash occupants in frontal crashes, while Figure 8 shows rib fracture frequency maps for occupants involved in side impacts. Lateral crashes tend to cause more rib fractures on the near side and are more posteriorly located than those observed in frontal crashes, where the rib fractures are distributed bilaterally and located more anteriorly in each rib. Using morphomics, we have been characterizing the changes in rib cage geometry with aging that may help to explain these findings. *[44-50]*

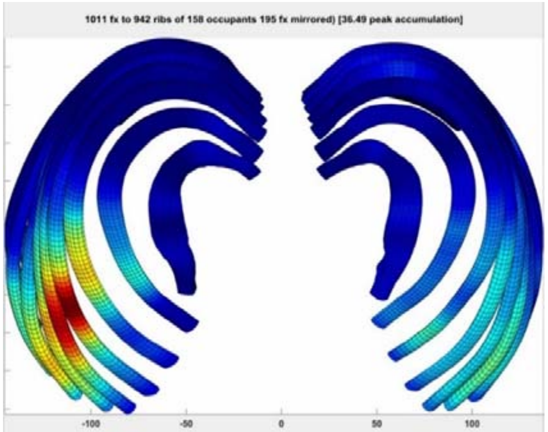

Figure 9 Rib Fracture Patterns in Frontal Crashes

Lower

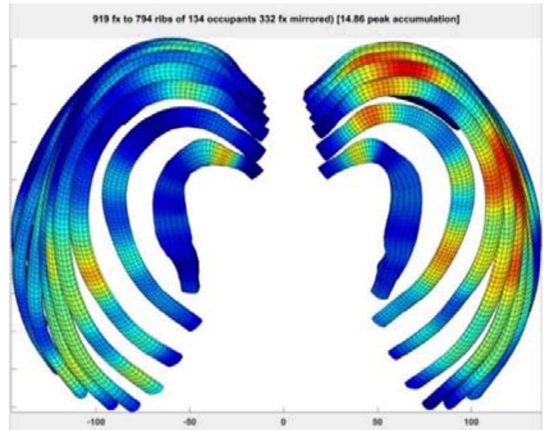

Figure 8 Rib Fracture Patterns in Side Impact Crashes

Extremity Injury

The obesity epidemic we have been observing worldwide over the past several decades is also contributing substantially to the morphomic variability of the population. (Figure 1) [6] While improvements in vehicle safety design have clearly decreased the incidence and severity of head and chest injuries in frontal crashes, lower extremity fractures have not decreased at the same rate and result in nearly half the lifetime costs associated with crash injuries. [51]

On initial univariate screening for lower extremity injuries in frontal crashes, we noted that longitudinal intrusion measures, as well as crash severity, were the most significant. This finding is consistent with conclusions from larger studies using NASS data, which we accept as ground truth. Measures of bone and muscle quality as well as weight were also prominent.

We next performed multivariate analysis to confirm the importance of the different classes of variables (vehicle, demographic, and morphomic) for the prediction of MAIS2+ lower extremity injury in frontal impact crashes. As we had data for the same morphomic measure at multiple vertebral levels, we selected values from one vertebral level only for inclusion in the model. We also selected morphomic variables to represent all the major body tissues (bone size, bone quality, muscle size, muscle quality, etc.) for inclusion in multivariate analysis. Logistic regression models were fitted using crash, demographic, and morphomic variables for occupants with and without MAIS2+ lower extremity injury as described above for chest injuries. We used four vehicle variables, three demographic variables, and six morphomic variables which resulted in over 8,000 models.

Using vehicle variables alone in the injury prediction model (Simple Model), the AUC was 0.763. With the addition of demographic factors, the AUC improved to 0.781. When morphomic variables were added to the vehicle variables, the AUC improved to an excellent 0.798. When all three types of variables (vehicle, demographic, and morphomic – Full Model) were included in the injury prediction model, the AUC was 0.807. Figure 10) One of the most important variables overall was BMI, confirming the importance of obesity in increased lower extremity injury risk. The observation that BMI was included in addition to the morphomic factors suggests that we did not fully capture the body variability due to BMI with the subset of morphomic factors included in the analysis. We are doing additional exploration to more fully characterize the morphomic changes that occur with obesity.

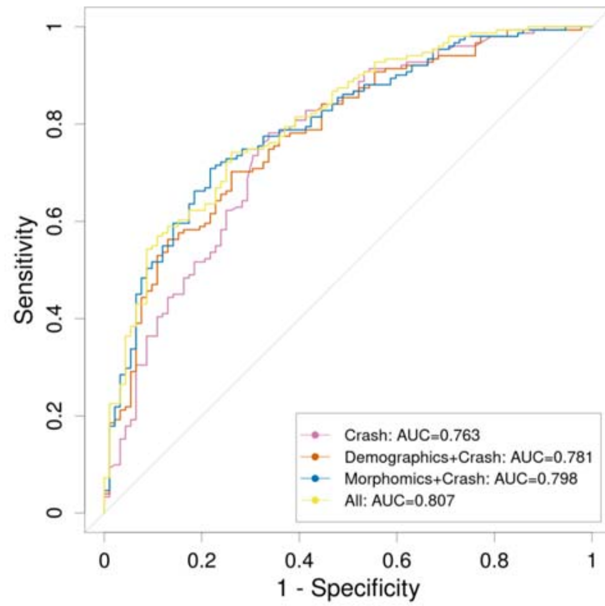

Figure 10 Prediction Performance of Models Using Vehicle, Demographic, and Morphomic Variables for Lower Extremity Injuries

Figure 11 summarizes the distribution of the morphomic factors identified to be significant for MAIS2+ lower extremity injuries for frontal crashes within the RAMP population. The figures are separated by gender and show the effect of age on the distribution and variability of each morphomic factor. The graphs show large variability in these factors that do not change as substantially with age or gender as did the morphomic factors found to be significant for lateral impact chest injuries.

In order to provide context for engineering and design efforts, we estimated the effect of differences in specific morphomic factors on MAIS2+ lower extremity injury risk for frontal crashes. For each morphomic variable, logistic regression was used to estimate the odds of MAIS2+ lower extremity injury. Confounding variables including Delta V, belt status, and gender were also controlled for in the logistic model. Odds ratios and risk ratios were calculated between 25th and 75th percentiles, 10th and 90th, 5th and 95th, and 1st and 99th of the morphomic variable for a belted male in a 25 mph crash-severity frontal crash. Similar trends were noted at other crash severities. Figure 11 and Figure 12 estimate the effect of differences in a single body factor on MAIS 2+ lower extremity injury risk. The figures highlight the differences in risk between a morphomically-50th percentile male and those at 1st, 5th, 10th, 25th, 75th, 90th and 95th, and 99th percentile.

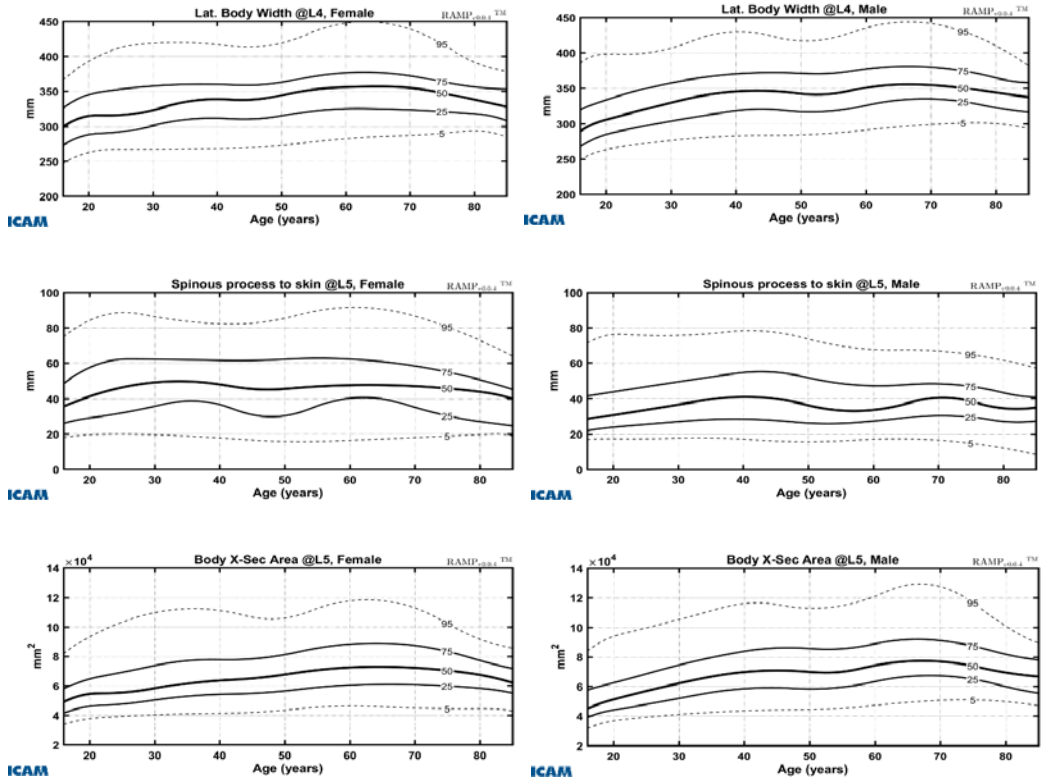

Figure 11 RAMP Charts for Morphomic Variables Predictive of Lower Extremity Injury in Frontal Impact Crashes

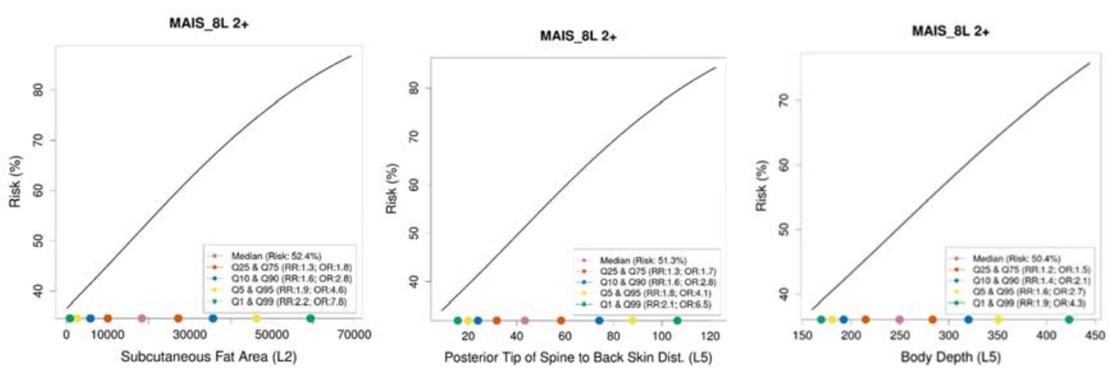

Figure 12: Effect of Subcutaneous Fat Area, Spine to Back Skin, and Body Depth Differences on Lower Extremity Injury Risk for a 25 MPH FRONTAL IMPACT Male, Belted

Summary

Bone and muscle quality, as well as body size are highly significant factors that predict whether a given individual will suffer thoracic injuries in a lateral impact motor vehicle crash. These observations are consistent with morphomic trends related to aging in the general population.

Body size measures, muscle quality, and fat distribution are significant factors that predict the severity of lower extremity injuries in frontal crashes. The body locations of the most significant morphomic factors suggest that current belt restraint system performance is degraded in the obese subpopulation.

Morphomic factors provide granular, quantitative data regarding body geometry and tissue quality. It will be important to define the relationship between tissue quality as assessed by morphomics and the material properties of those tissues. Morphomic factors can then guide the development of biofidelic test devices as well as finite element models, deterministic and stochastic, that better represent real-world crash occupants. Such advances will enable the development of adaptive restraint systems that optimize crash protection for a greater portion of the population at risk.

Conclusion

Individuals within a population vary greatly. This variation in body size and condition affects the severity and pattern of injuries they suffer in motor vehicle crashes. If we are to increase the precision and effectiveness of vehicle safety countermeasures, this variability within the population must be taken into account and addressed proactively. As I learned early in medical school, treat the patient and not just their disease.

Epilogue

It is a tremendous honor as a surgeon to have an opportunity to address this august gathering of injury biomechanics and vehicle safety professionals. Over the past two decades, I have learned immensely from my collaborative interactions with members of this community. Our interdisciplinary research led to the invention of analytic morphomics and to insights and techniques that enable us to translate between our medical and engineering disciplines.

While morphomic measures of body condition are important predictors of fragility or injury severity following a traumatic event, we have also found them to be significant predictors of clinical outcome following medical treatment. The body is the Biological Medical Record of each individual and the body is what a physician treats when a medical need arises. For example, surgeons frequently struggle to determine patient suitability for liver transplantation. We hypothesized that objective measures of overall body condition, such as low muscle mass/function (sarcopenia), could inform clinicians and help avoid futile or harmful operations. After controlling for donor and recipient characteristics using Cox regression models, we found a strong association between psoas area and post-transplantation mortality (hazard ratio = 3.7/1,000 mm2 decrease in psoas area; $p < 0.0001$). When stratified into quartiles based on psoas area (holding donor and recipient characteristics constant), 1-year survival ranged from 49.7% for the quartile with the smallest psoas area to 87.0% for the quartile with the largest. The impact of psoas area on survival exceeded that of all other covariates in these models. [52]

We also used core muscle size as an objective measure of frailty and predictor of survival after abdominal aortic aneurysm (AAA) repair. Cross-sectional areas of the psoas muscles at the level of the L4 vertebra were measured. Cox regression revealed a significant association between psoas area and postoperative mortality ($P = .003$). Among all covariates included in the Cox models (including predictors of mortality such as American Society of Anesthesiologists [ASA] score), the psoas area was the most significant. [53]

We used these findings as motivation to begin training our patients before surgery. We have found that several weeks of incentivized walking (along with breathing exercises, smoking cessation and stress reduction) substantially reduced postoperative complications, hospital stay and medical costs. [54,55]

We have also looked at the association between cancer survival and morphomics and found that we can detect differences in morphomic factors that predict cancer progression and survival. [56-59]

The availability of pristine CT scans in radiologic archives have made it possible to extract massive volumes of morphomic data about a subject’s body condition at the time of their injury or surgery, even if that event was many years in the past. This morphomics data, when coupled with injury information and even rudimentary data about the traumatic event, was able to help predict an individual subject's injury risk. Similarly, morphomic factors extracted from CT scans were highly significant in models to predict clinical outcomes following surgery (a controlled traumatic event). In our experience analyzing fragility and frailty in multiple clinical populations, morphomic data extracted from medical imaging scans have consistently added substantial as well as novel predictive value. This ability to more granularly measure individuals and determine where they fall within a heterogeneous population is the essence of precision medical treatment and prevention.

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