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Editorial

Adaptive Bone-Remodeling Analysis

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Wolff's Law and the Orthopaedic Surgeon

I surmise that there is no single issue so central to the scientific basis of Orthopaedics as Wolff's Law. And yet, the work of Wolff is hardly red by Orthopaedic residents, hardly taught in medical shools and, yes, hardly understood by those who are meant to apply it. In Orthopaedics, Wolff's Law is passed on from generation to generation like a historical legend. If the implications of Wolff's Law are so important, which no one in this field would probably doubt, then why is it not the subject of rigorous study and application? «Wolff's Law» or the «Law of Bone Transformations» is rather pretentiously formulated, but it does not explain how bones transform, nor does it predict to what bones transform. It is based on the observations of similarity between trabecular structure and stress trajectories calculated in Culmann's crane, from which the hypothesis is deduced that bone transformations are governed by the same mathematical laws as those on which the above similarity is based. Whatever those laws may be. In the development of Orthopaedics, «Wolff's Law» became a trunck in which many conceptual ideas were packed. As Roesler[1] (1987) wrote «...the trajectorial hypothesis of Wolff[2] (1870, 1892), the theory of functional adaptation of Roux[2] (1881), and the maximum-minimum principle originated by Bourgery[2] (1832) or Bell[2] (1834) by repeated and unchallenged use in the literature and in research, amalgated to «Wolff's Law», that «like a *deus ex machina* explained the otherwise inexplicable, if required» (Kummer,[2] 1985)...». From a practical point of view, we have little more to work on than the general principle that bones tend to loose mass when understressed and gain mass when overstressed. This general principle is frequently confirmed in the clinic and used as a basis for many Orthopaedic treatment modalities. Apart from this general principle, there is no such thing as a «Law for Bone Transformation». So there is little to read, teach or understand, rather than the, indeed interesting and sometimes amazing, historical documents. Still, on the one hand, never in history has the need for such a law been greater than at the present. This is due largely to the popularity of implants. To put it simply, bones transform, but implants do not. We will never be able to define optimal implant materials and shapes as long as we cannot predict how they will interfere with the bone-transformation mechanism. On the other hand, the chances that such a law will emerge from science, have never been greater than at his particular moment. Not because we are smarter than our predecessor, but because we can stand on their shoulders and we have better experimental and analytical research tools at our disposal.

The stress trajectories in Culmann's crane, from which Wolff derived his trajectorial hypothesis, were calculated with «graphic statics», at that time a new method of civil engineering mechanics. We now also have a new tool from engineering mechanics to analyze bones: the finite-element method. I predict that the application of this method to the question of bone transformation, combined with quantitative bone-remodeling theories in computer-simulation models, will create a similar historical landmark in our time and age, as the application of graphic statics did in the last century. I also dare to foresee, that a genuine, quantitative law, explaining both structure and transformation of bones, will soon emerge from it.

Bones as optimal mechanical structures

That bones are optimal mechanical structures is an unchallenged axiom. The question is, however, for what they are optimized. Are they optimized to provide «efficient» load transfer; that is to say, adequate strength for the functional loads required with a minimum amount of material used? Or is rigidity the optimization target, rather than strength? Are they uniform strength structures; that is to say, are the risks for local fractures equally divided throughout a bone? Or are they rather uniform strain or uniform stress structures, meaning that every part of the bone experiences an equal amount of local maximal deformation or stress? Whatever the answer may be, the laws of

mechanics dictate that, given particular loads applied to a bone, its strength characteristics, stress and deformation patterns depend on its external shape, its internal structural organization and on the mechanical properties of its ground substance, the materal of which it is composed. If we consider the ground substance as a given entity per individual, with particular elastic properties and strength characteristics, then there are two independent factors left: shape and internal structure. The concept of bone as optimal mechanical structures then implies that there is a particular (natural) balance, in each bone, between loads, shape and internal structure. So if, for example, a bone is optimized to provide maximal rigidity, using a minimal amount of ground substance, this simply means that the shape and internal structure were mutually adjusted in such a way, that these goals are realized for the particular loads to which the bone is exposed.
By describing the problem of bones as optimal mechanical structures in this way, we make it accessible to quantitative analysis. In a finite-element model, for instance, it is quite feasible to represent external loads quantitatively, and also to describe shape and internal structure mathematically. When this can be done accurately, the model provides us with a complete description of the stresses and strains that occur throughout a whole bone. We could then, for instance, check whether bones are uniform stress structures (they are not!). This does not imply that the problems are solved, but they can be defined and classified more clearly: what are the external (muscle and joint) loads for a particular bone? What are the mechanical (elastic) properties of the ground substance? How can we describe the internal structure mathematically? What is the mechanical optimization target? A more fundamental question is, whether the optimal combination of shape and internal structures is defined in our genes, or if we are programmed only with the optimization target. In other words, whether the optimal, natural balance has been generated in the process of evolution, or whether each individual must develop it again, based on the loads applied to the bones during growth and daily activity. If the former is the case, then the transformation mechanism is aroused only when disturbances in load, shape or internal structure occur. If the latter is the case, then it implies that the actual shape and structure form a state of dynamic equilibrium and may be adjusted continuously.

Bone tranformation as a biological control mechanism

The natural, optimal balance between loads, shape and internal structure is disturbed when one of these suddenly changes. Such a disturbance may be caused by a change in lifestyle which affects the loads, but also by the placement of an implant, which changes the internal structure where metal takes the place of bone. The concept of functional adaptation or transformation implies that the bone would then adapt its shape and internal structure to find a new balance, which again realizes the optimization target. This can only happen if there is an adaptive biological control mechanism. This control mechanism must be suited to measure the mechanical requirements to which the bone tissue is exposed on the one hand, and regulate bone mass accordingly on the other. The question is, how is it composed, how does it work, and where is it located? It is possible that this control mechanism operates locally in the bone. Hence, that every little chunk of bone measures its own local mechanical load and regulates its own mass independently; that there is no direct interference from the neuro-sensory system and no direct communication between different parts of a bone. This is the hypothesis of bone as a self-optimizing material. It is by no means an unchallenged certainty, but I nevertheless use it as an axiom here.
The hypothesis implies that, distributed throughout the bones we must have *sensors* (e.g. osteocytes or lining cells), which continuously measure an internal loading variable or mechanical *signal* in their own environment (e.g. stress, strain or some other mechanical variable). When the signal is not within a certain range, i.e. too high or too low, the sensors, through some kind of biochemical mediator, invigorate *actors* (osteoclasts and osteoblasts) to regulate bone mass, again in the environment of the sensor. This hypothetical control mechanism is illustrated in Figure 1. Again, like in our discussion of bones as mechanically optimized structures, this biological model enables us to approach the process of adaptation analytically. The fundamental questions here are those relative to the nature of the signal, the value which represents the natural balance, and the mathematical relationship between signal and bone-mass adaptation. There is certainly a direct mechanical relatioship between this biological control model and the structural bone concept discussed earlier: the signal each sensor measures depends on the external loads, shape and internal structure of

the whole bone, whereas the local bone mass around each sensor again contributes to the global shape and internal structure.

Finite-element based computer-simulation models

In a finite-element model of a bone, loads, shape and internal structure must be represented. The former two present no principle problems for the finite-element model, but internal structure is difficult to handle. The problem is, that there are so many different levels of organization, from the macroscopic to the submicroscopic. To simplify things to some extent, let us just consider the highest level of structural organization, the «supramacroscopic» one; that is, as we see bones on radiograms. All we can really see on a radiogram is a density distribution. We know the highest density represents cortical bone, and the lowest trabecular bone. The latter is porous, and the higher the porosity, the lower the density. We do not really see the pores, just the variable shades of density. So we have now created a conceptual model of bones as mechanical structures, characterized in their mechanical properties by external shapes and internal density distributions. Hence, in the finite-element model, each element is assigned a particular density value (an amount of bone mass per unit volume, with cortical density as a maximum) and this density value is automatically coupled to a value of the elastic modulus; the higher the density, the stiffer the bone element, hence the higher the elastic modulus.

The next step is to describe the adaptive biological control mechanism mathematically, the regulation of bone mass in the environment of a sensor cell. Such an environment is represented in the finite-element model by an element. In other words, every element is supposed to have one sensor cell. The amount of bone mass in the element is denoted by M. Then dM/dt denotes the amount of net bone mass turn-over per unit of time. This either implies an increase (dM/dt is positive) or a decrease (dM/dt is negative) of the density in an element (with cortical density being the maximum), and growth (dM/dt is positive) or shrinkage (dM/dt is negative) of an element, if it is located at the surface. The mechanical signal which the sensor is supposed to measure is denoted by S, whatever it may represent. As explained earlier, the concept of bone as a self-optimizing material implies, that the mechanical signal (S in this case) is equalized to some pre-arranged value, an optimization target, by addition or removal of mass. This pre-arranged value is denoted by k. The optimization target can then be expressed as S=k, hence the mathematical remodeling rule becomes

$$\frac{dM}{dt} = C\,(S-k)$$

where C is some kind of constant physical parameter. The formula simply states mathematically that when S equals k in an element, hence when the mechanical signal is normal, dM/dt equals zero, hence no net addition or removal of bone in the element concerned. It also states that while S is higher or lower than k, addition or removal occur until S is again normalized. In this process, the rate of change is directly proportional to the degree of abnormality, i.e. the difference between S and k.

Combined with the finite-element model, this produces a computer-simulation model for adaptive bone remodeling as illustrated schematically in Figure 2. What this simulation model could produce, conceptually, is amazing. When we provide it with an initial shape, an initial density distribution, and with particular loading conditions, it will adapt the shape and the density distribution to meet the optimization goal, S=k, as good as possible. This produces a particular shape and density distribution, the characteristics of which depend on the (unknown) nature of the signal S we have selected and on its normal, target value k. Hence, using an inverse, empirical approach, we can vary S and k in a process of trial and error until realistic results are produced by the computer simulation model.

Application to bone structure

This process of «trial-and-error» was performed relative to the proximal femur, whereby a number of additional simplifications were introduced, just to make things a bit easier: (i) we considered the external shape as a given, non-adaptive entity (hence, only the density is allowed to change), (ii) we assumed that three different loading cases represent the loading history of «daily activity«, and (iii) we only considered a two-dimensional, mid-frontal slice of the bone, with two-dimensional

loads. We assumed that the optimization target k of the mechanical signal S is one single constant for the whole bone; hence k has the same value in all elements. After much trial and error, we choose the elastic energy per unit of mass as the mechanical signal, following a suggestion from Carter and associates in Stanford, CA. Hence, in the model, the signal S is equal to the average elastic energy stored in an element as an effect of the loads, divided by the amount of bone mass in the same element. More «trial-and-error» produced the best value for the target value k, and the end results, the predicted density distribution, is shown in Figure 3. It is truly amazing, that such a self-optimization process, whereby each element works for itself to realize its optimization notwithstanding, this result is quite realistic. The most important characteristics of the real femur are apparent in the prediction: the intramedullary canal, the cortices, Ward's triangle, the cortical shells and the characteristic density patterns in metaphysis, the greater trochanter and the femoral head. The solution also gives indications suggesting that the predicted density distribution has minimal total weight, hence that it is an efficient solution. The conclusion is, that the proximal femur seems to be a mechanically optimized structure relative to a uniform elastic energy distribution per unit of mass, combined with minimal weight. A preliminary conclusion, surely, but nevertheless an important one.

Application to bone adaptation

In another example we simulated animal (canine) experiments with total hip replacements, carried out in the Chicago group of Galante and associates. The prosthesis (the femoral stem) changes the internal structure of the femur by replacing bone by metal. This disturbs the natural, optimal balance between loads, shape and density distribution. Hence, given similar function pre- and postoperatively (hence similar loads), shape and density are transformed, adapted, to find a new balance whereby the signal value in each element is again equalized to its target valute k. In this case we do not have to worry about the value of k, because we can simply calculate it, per element, in a finite-element model of intact bone. Again elastic energy per unit of mass was used for the signal, but this time the finite-element model was three-dimensional and both adaptation of density and shape were allowed. In Figure 4 we see a comparison between animal experimental findings after two years follow-up and predictions of the computer-simulation model. The adaptation of both cortical area and trabecular density are predicted with quite acceptable accuracy, even in detail. This implies that the bone adaptive processes around implants can be simulated and their long-term effects predicted. Hence, we do not necessarily have to wait 10 years or longer to assess the long-term consequences of particular prosthetic design features on bone remodeling and resorption. We can estimate those consequences already in the conceptual design phase of an implant. Whether it concerns a new material, an innovative shape or alternative coating configurations, the question of how it interferes with the bone adaptation process can be addressed even before the first clinical trial has begun.

Closing remarks

The examples presented are, of course, only the first efforts to explain structure and adaptive remodeling of bones quantitatively, using finite-element based computer-simulation models. Many questions are as yet unanswered, but at least they can be well defined within the context of the conceptual model. It is essential to appreciate the hierarchy in the arguments, assumptions and simplifications I discussed before actual quantitative predictions were presented. The notion that the mechanical behavior of a bone depends on its shape, internal structural organization, the mechanical properties of its ground substance and on the external loads to which it is exposed, is a conceptual one. The same is true for the idea that shape and internal structure are balanced according to some optimization target, which is maintained by a biological control mechanism operating locally in the bone, using sensors to assess load and actors to regulate bone mass. These are conceptual prerequisites for the rest of the course. On a lower hierarchical level are the assumptions made in the process of describing the conceptual model mathematically, like the representation of daily activity by a finite number of characteristic loading cases, and the representation of the remodeling signal by elastic energy per unit bone mass. The validity of these assumptions must be investigated fur-

ther. But if they prove untrue or inaccurate, it would not invalidate the approach as a whole, it only implies that alternative assumptions must be considered. On the lowest hierarchical level are the assumptions made simply out of convenience in the present examples, like the particular form of the mathematical remodeling rule or the restriction to a two-dimensional finite-element model. This may be inaccurate, but has no serious consequences for the method as such.
A conclusion to the effect that Wolff's Law has now been quantified would be premature. Much work is still to be done. But certainly, the results that we and others have hitherto produced with these methods are very promising indeed. They already provide useful explanations for phenomena seen clinically. The prospects for the future are exciting.

1. Roesler H. (1987). The hystory of some fundamental concepts in bone biomechanics. J. Biomechanics, 20:1025-1034.

2. See Roesler (1987).