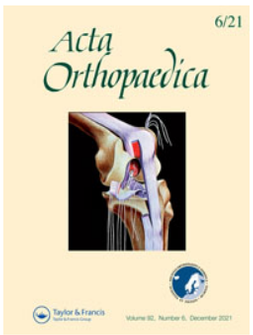

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Guest editorial: Imaging bones of contention

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Guest editorial

Imaging bones of contention

Readers naturally are impressed by the colored sections of computed anatomical registrations of physiological and, by extension, pathophysiological variables in vivo, known as tomograms. The technique is not really new, but recent technological advances have improved its perceived applicability to the solution of important clinical problems. The results are spectacular at best, promising on average, and less than suggestive at worst.

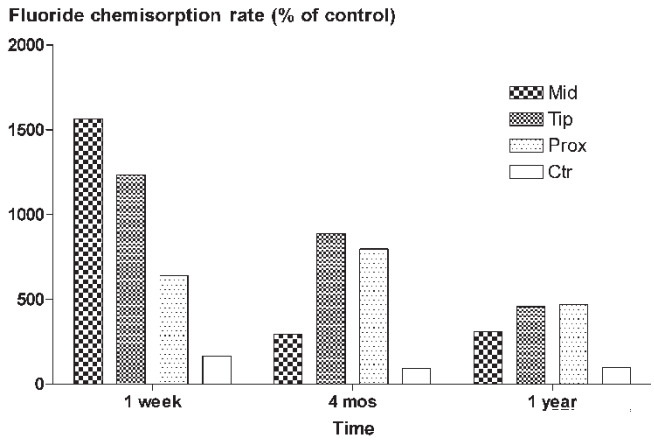
Positron emission tomography (PET) and the novel hybrids of PET-CT and more recently also PET-MR are virtual windows on the dynamic processes of living bodies. If the fulfillment of the promises has been slow in coming, it is first and foremost because the equipment, including a cyclotron, is expensive, next because the analysis of the results can be both complex and time-consuming, and last, but certainly not least, because the interpretation is fraught with misunderstanding. Practitioners of PET endlessly debate the relative merits of measures, such as SUV, clearance, rate constant, flux, binding potential, volume of distribution and other variables from the physiological arcana.

As the product of clearance and concentration, flux is more informative and biologically relevant than concentration, they argue. While a concentration largely is meant to remain constant in life, a flux must vary continuously in response to the exigencies of life by adjustment of its underlying clearance. Flow is a clearance, albeit with an extraction fraction of unity, as is the slope of the Patlak plot. Clearance, in turn, is the product of volume and rate.

The final analysis is all about volumes and rate constants, the essence of which tempts us with its artificially cleansed kinetics. The spectre of compartment theory haunts many PET investigations in which methodological issues detract from an important clinical observation. If PET researchers are unsure whether an unsolved clinical problem can be addressed with a valid method, or whether a disputed method should be evaluated by a well-understood clinical case, they often attempt lamely to do both in a single study, with unsatisfactory results. It is understandable that some potential users refuse to wait longer for the verdicts; for them the PET practitioners must do their business, as the Americans say, or get out of the way.

In "Rapid bone and blood flow formation in impacted morselized allografts", published in this issue (pp 633–43), Sörensen et al. report novel observations made with generally accepted PET methods, but methodological questions affecting the interpretation still arise from the findings. The fluoride ion ($^{18}F^-$) of the positron-emitting isotope fluorine-18 was the first PET tracer to be officially approved for bone imaging by the FDA as early as in 1972, 10 years after its first introduction as a new isotope for bone scanning (Blau et al. 1962). The tracer fluoride ion is known to accumulate at sites of osteoblastic reactivity by exchange with the hydroxyl groups of hydroxyapatite crystals and formation of [^{18}F]fluoroapatite. The accumulation reflects the essentially unidirectional chemisorption that traps the tracer fluoride ions in competition with washout from the extravascular space. To identify the time of most active formation of bone after impaction of frozen allografts in revision of total hip arthroplasty, Sörensen et al. measured tracer fluoride ion clearance at intervals. Because the interpretation depends on the blood flow, the authors also measured blood flow and blood volume with tracer water and carbon monoxide labeled with the positron-emitting isotope oxygen-15.

Here the endlessly debating PET practitioners may have a point; there are good reasons for the multiple tracers. In isolation, the clearance of tracer fluoride yields equivocal answers to the



Osteblast activity after grafting

question of new bone formation, depending on the delivery of the tracer by the circulation. An upper limit of accumulation is reached when the concentration in the extravascular space is depleted by chemisorption so intense that blood flow rather than the amount of hydroxyapatite determines the incorporation. Uncorrected for blood flow, SUV or clearance can mask the most important results of a study. In the present case, the analysis of Sörensen et al. fails to do justice to the exciting result that the rate of chemisorption in fact is increased more than 15-fold in the MID region of the images as early as one week after the grafting.

To obtain this result it is necessary to consider the slope of the Patlak plot, which equals a specific combination of the unidirectional clearance and compartmental rate constants of the underlying compartment model. Piert et al. (1998) measured the unidirectional plasma clearance of tracer fluoride ions to be 80% of the blood flow, and Hawkins et al. (1992) found the whole-blood concentration of tracer fluoride to be 80% of the plasma concentration. Together the two findings show that the permeability of the capillary wall to tracer fluoride ions is so high that the plasma clearance of the tracer can be assumed to be close to 80% of the blood flow at all times. The rate constant of washout is the unidirectional plasma clearance relative to an extravascular distribution space, which is likely to be close to 20% of the tissue volume. Now joint measurements of both blood flow and net plasma clearance allow the rate of chemisorption to be calculated as $KF/(0.2F–0.25K)$, where K is the net clearance of tracer fluoride ions and F is the blood flow. The calculation reveals a more marked increase of the chemisorption rate one week after the grafting than suggested by the SUV or clearance alone, as shown in the Figure.

The bad news is that the equivocation does not end here, The estimates of chemisorption in turn are subject to evaluation because the rate is the product of the number of hydroxyapatite chemisorption sites and the rate of bimolecular association of tracer fluoride ions with the hydroxyapatite crystals, relative to the physical volume of distribution of untrapped tracer fluoride ions, all of which could in principle change with the surgical intervention and the passage of time. The good news is that each step brings us further away from ignorance.

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Blau M, Nagler W, Bender M A. A new isotope for bone scanning. J Nucl Med 1962; 3: 332-4.

Hawkins R A, Choi Y, Huang S C, Hoh C K, Dahlbom M, Schiepers C, Satyamurthy N, Barrio J R, Phelps M E. Evaluation of the skeletal kinetics of fluorine-18-fluoride ion with PET. J Nucl Med 1992; 33: 633-42.

Piert M, Zittel T T, Machulla H J, Becker G A, Jahn M, Maier G, Bares R, Becker H D. Blood flow measurements with [^{15}O]H_2O and [^{18}F]fluoride ion PET in porcine vertebrae. J Bone Miner Res 1998; 13: 1328-36.