assist in the prevention of delayed union.[5-7] On the other hand, increased sketelal loading through exercise has been shown to increase bone mass.[8,9] Conversely, subnormal mechanical stress as a result of bed rest or immobilization, results in decreased bone density and disuse osteoporosis.[10-12] Recently, results from spaceflight studies demonstrated that microgravity has negative effects on the skeleton.[13-16] It can affect gene expression in bone and muscle. Both osteocalcin and the prepro-$\alpha2$ chain of type I precollagen mRNA levels decreased in long-bone and calvarial periosteum after spaceflight.[17] In addition, mineral resorption, as measured by ^{45}Ca release, increased during a 4-day culture period in space.[18] These data indicate that weightlessness has modulating effects on bone tissue cells.

Influence of Force Factors on Bone Remodeling

Although the precise mechanisms are not fully understood, it is clear that there are many characteristics of the force, including the magnitude, rate of change and applied duration which may be involved in controlling cellular behavior. In the past two decades, numerous studies discussed the effects of load bearing on bone remodeling using static[19] and dynamic loading.[20-22] By comparing the bone area on the periosteal surface of the ulna of turkeys, Lanyon and Rubin found that a static load sufficient to produce strains in the functional dynamic strain range has no effect on bone remodeling, whereas a similar load applied intermittently for a short daily period may be associated with a substantial increase in bone mass.[23] On the other hand, experimental results in mammals have demonstrated that bone formation rates show highly significant correlations with the duration, peak value, and number of cycles for which bone is loaded.[24] Also, across the physiological range, a high rate of strain change on bone provides a greater osteogenic stimulus than does the same peak strain achieved more slowly.[25,26] These results indicate that the mechanical environment is a major determinant of the physiological behavior of mammalian bone tissue.

While investigating the mechanotransduction phenomenon, Gross and Rubin found that increased bone formation does not always occur near the tissue where deformation is the greatest.[27] In a series of animal studies, Turner et al. found that the bone formation rate (BFR) did not increase by loading at lower loading frequencies, but increased significantly at higher frequencies; furthermore bending significantly increased the relative BFR compared with sham loading.[28] Results obtained from a cell level study showed that bone cells also respond to fluid shear forces like endothelial cells do.[29] These results suggest that bone cells do act as sensors of the indirect effects of tissue deformation-interstitial fluid flow.

The Role of the Lacuno-canalicular System

The cellular response mechanism of bone tissue remodeling must start with an adequate mechanical signal that is detected by sensor cells, leading to generation of an adequate chemical signal that modulates bone formation and/or bone resorption. Both osteoblasts and osteocytes were discussed as a candidates for the sensor cell;[30-32] however, it has been shown that the response of osteoblasts to such mechanical strain is smaller than that of osteocytes.[33,34] Therefore, osteocytes seem to be the major sensor cell which responds to mechanical stimulation.[31]

Although knowledge of osteocytes has existed since the 19th century, little is known about the functions of these cells. This is because osteocytes are confined within the calcified matrix. Due to the lack of a method to isolate osteocytes, in vitro study of the cell was not possible until osteocytes were identified in osteoblast-like cell cultures using the monoclonal antibody (MAb), OB 7.3.[35-37] Recently, cellular studies demonstrated that osteocytes indeed are the most mechanosensitive cells in bone involved in the transduction of mechanical stress into a biological response.[38] According to these experimental results, a theory was proposed that the mechanisms by which osteocytes respond to mechanical stimulation are strongly correlated to the lacuno-canalicular system.[31,39-41]

Osteocytes are encased in calcified cavities, i.e. lacunae, and communicate to each other by means of gap junctions in the canalicular system.[42,43] Osteocytes can receive nourishment and remove waste products through fluid transport in the lacuno-canalicular system. As shown in Fig. 1, when a beam-like structure is subjected to a bending load, compression and tension stresses can be found symmetrically in a concave pattern on the downward side and in a concave upward side, respectively. Theoretical model simulations have demonstrated that fluid flow can occur from regions of