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Design and preliminary testing of an active intramedullary nail

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ABSTRACT

Purpose. To enhance bone healing through controlled interfragmentary movements, numerous experiments have been conducted in animal models employing external fixation devices to apply mechanical stimulation to the fracture site. However, the efficacy of these fixators has been questioned. On the other hand, intramedullary nailing is a widely established clinical practice for reducing closed tibial fractures. **Material and methods.** In an effort to enhance bone healing, to overcome the disadvantages of external fixators (i.e., non-uniform linear movement), and to enhance the advantages of intramedullary nailing (i.e., reduced risk of infection), an active intramedullary nail has been designed and fabricated. Active nail will provide controlled *in-situ* stimulation (simultaneously axial and shear) from a selectable acceleration (0.35 to 8.17g – axial and 0.44g to 10.46 g - shear), associated to a discreet set of high-frequency values (29.82 - 172.05 Hz - axial and 29.68 to 172.13 - shear). **Results.** Five active intramedullary nails were fabricated, capable of producing average acceleration between 0.35 and 10.4 g. Acceleration is applied simultaneously by all three axes (x, y, and z), resulting in axial and shear stimulation. For each acceleration level, there are a limited number of frequencies that can be selected. For each frequency, there are a limited number of acceleration levels that can be delivered. Bone morphology produces different levels of acceleration in each axe. Acceleration levels are controlled externally only by the variable power source ($1.5V_{DC}$ to $6V_{DC}$). Accelerated *in-vitro* testing showed that the life of the device exceeded the required active period. Mechanical test showed that in case of failure of the active component, the active intramedullary nail will act as a standard nail, allowing bone healing to continue its normal course. *Ex vivo* experiments were conducted inserting one active intramedullary nail in two intact adult sheep tibia. Results indicate that the strain induced by the active intramedullary nail (from 18.62 $\mu\varepsilon$ to 38.13 $\mu\varepsilon$) has been reported to be osteogenic. Additional experiments are required in order to statistically validate the strain that can be induced *in vivo* by the active intramedullary nail. Also, *in vivo* experiments using simple fractures of the tibial shaft need to be conducted in order to assess

Diseño y pruebas preliminares de un clavo intramedular activo

RESUMEN

Propósito. *Numerosos autores han reportado la aplicación de estimulación mecánica a fracturas óseas (movimientos inter-fragmentarios) con el propósito de acelerar la reparación ósea. Para aplicar esta estimulación al sitio de fractura se han utilizado fijadores óseos externos; sin embargo, la eficacia de los fijadores externos ha sido cuestionada. En comparación, el uso de clavos intramedulares pasivos para la reparación de fracturas es una práctica clínica ampliamente utilizada.* ***Material y métodos.*** *Con el propósito de acelerar la consolidación ósea sin las desventajas que presentan los fijadores externos (por ejemplo, movimiento lineal no uniforme), y al mismo tiempo mejorar las ventajas de los clavos intramedulares (por ejemplo, menor riesgo de infección), se diseñó y se fabricó un clavo intramedular activo que proporciona estimulación mecánica* in situ *(axial y cortante). Los parámetros de estimulación se seleccionan de un conjunto discreto de valores de aceleración (0.35 g a 8.17g - axial y 0.44 g a 10.46 g - cortante), asociado a un conjunto discreto de valores de amplitud (29.82 a 172.05 Hz - axial y 29.68 a 172.13 - cortante).* ***Resultados.*** *Cinco clavos intramedulares activos fueron fabricados. Los dispositivos produjeron una aceleración promedio de 0.35 a 10.4 g. La aceleración se aplica simultáneamente en los tres ejes a través de una fuente de poder variable ($1.5V_{DC}$ a 6 V_{DC}) resultando en estimulación mecánica axial y cortante. Para cada nivel de aceleración existe un número limitado de frecuencias que puede ser seleccionado. Para cada valor de frecuencia existe un conjunto discreto de valores de amplitud que pueden ser seleccionadas. La morfología ósea resulta en diferentes valores de aceleración en cada uno de los ejes. Pruebas aceleradas* in vitro *mostraron que la vida del dispositivo excede el tiempo requerido de funcionamiento activo. Las pruebas mecánicas mostraron que en caso de falla del elemento activo, el clavo intramedular se comporta como un clavo intramedular convencional por lo que el proceso de* if effectively, applying active mechanical stimulation *in situ* enhances bone healing.

consolidación ósea podrá concluir sin intervenciones adicionales. Se llevaron a cabo experimentos ex vivo *colocando el clavo intramedular activo en dos tibias de borrego adulto (macho Suffolk 100 kg). Los resultados indican que la deformación producida por el clavo varía entre 18.62 $\mu\varepsilon$ y 38.13 $\mu\varepsilon$. Estos valores de deformación son osteogénicos, según reportes de la literatura. Se requiere llevar a cabo experimentos adicionales para validar estadísticamente la deformación que induce* in vivo *el clavo intramedular activo. De igual forma será necesario llevar a cabo experimentos* in vivo *utilizando un modelo animal de fracturas simples para determinar si la aplicación* in situ *de estimulación mecánica acelera la consolidación ósea.*

Key words. Bone healing. Mechanical stimulation. Active intramedullary nail.

Palabras clave. *Consolidación ósea. Estimulación mecánica. Clavo intramedular activo.*

INTRODUCTION

The rate, quality, and progression of bone repair is modified by the rigidity of cast immobilization, stif-fness of fixation, control of weight bearing, and applied loading to the fracture site.[1,2] According to several authors,[6-9] relative interfragmentary movement is present at the fracture site. Axial compression and shear develops as a result of combined movement and twisting of the bone fragments.[8,9] Thus, if appropriate loading to the fracture site is applied, it will promote the healing response,[3,4] however, if too much load is applied, it can inhibit the healing process.[5]

In an effort to assess the possibility of improving bone healing through controlled interfragmentary movements, numerous authors have used animal models to study the effects of mechanical stimulation on fracture healing.[10-16] Goodship, *et al.* (1985)[1] suggested that early micromovement increases bone mineral density and stiffness when stimulation is applied early *vs.* when it is applied late. Goodship, *et al.* (1998)[12] further reported that high strain rates with shear motion increase callus formation in pigs if stimulation is applied early, and that these inhibit healing progress if the same stimuli are applied after 8 weeks.

All of the authors cited previously have utilized external fixation devices that were selected according to animal size. However, several authors have questioned the efficacy of these fixators.[17] Claes *et al.* (1995)[18] describe how unilateral external fixators apply non-uniform motion, altering the axial component applied to the bone, thus reducing the efficacy of fracture dynamization.

On the other hand, intramedullary nailing is a widely established clinical practice to reduce closed tibial fractures. Multiple authors[19-22] suggest that intramedullary nailing may yield better outcomes. Some of its advantages include better control of alignment, improved mobility of the patient, and the patient's earlier return to work.[23] Experts consider implantation of interlocking intramedullary nails as the method of choice for unstable tibial shaft fractures.[21,24,25]

The aim of this study was to design an active intramedullary nail that would enhance the advantages of intramedullary nailing (better control of alignment, improved mobility of the patient, and reduced risk of infection). We planned to accomplish this task by designing and developing an intramedul-lary active nail that would provide controlled low-magnitude, high-frequency *in situ* stimulation (axial and shear) to the fractured bone.

MATERIAL AND METHODS

To develop the experimental device, the following steps were established:

- Determine desired functional and safety characteristics of the new device.
- Design and prototype fabrication.
- Mechanical performance tests.
- *In vitro* tests.
- Mechanical strength tests.
- *Ex vivo* characterization.

Desired functional and safety characteristics

- **Materials.** All materials in contact with the body should be biocompatible (ISO 10993-1, Sections 3.1 to 3.4).[26] All metallic intramedullary nailing systems should comply with ISO 15142 Part 1.[27]
- **Size.** The mechanical stimulus device should fit within the lumen of an intramedullary nail in or-

der to maintain the surgical procedure as similar as possible to the actual fracture-reduction procedure utilizing intramedullary nails. For the prototype, a 9 mm OD nail was selected.

- **Nail load resistance.** The prototype nail should resist the same load as that of a static nail of similar diameter and geometry. It must comply with standard ASTM F1264 -03 part A1 (Test method for static four-point bend test method).[28]
  The active nail should perform as a static nail if malfunction were to occur during the experimental phase.
- **Mechanical stimulation characteristics.** The active nail should be capable of delivering control-led acceleration initiating at 0.3 g[29-31] and at a controlled frequency range from 10-150 Hz. This is a wider range of frequencies than reported in the literature.[29-31]
- **Vibration duty cycle.** The device should be capable of delivering the selected acceleration and frequency for a minimum of 2 weeks, 5 days per week, 20 min per day.[31,32]
- **Leakage current.** If the mechanical stimulator devices to be used were electric, the new intramedullary nail should comply with norm IEC 60601-1-1 3rd ed. (clause 8.4.7.4.h).[33]

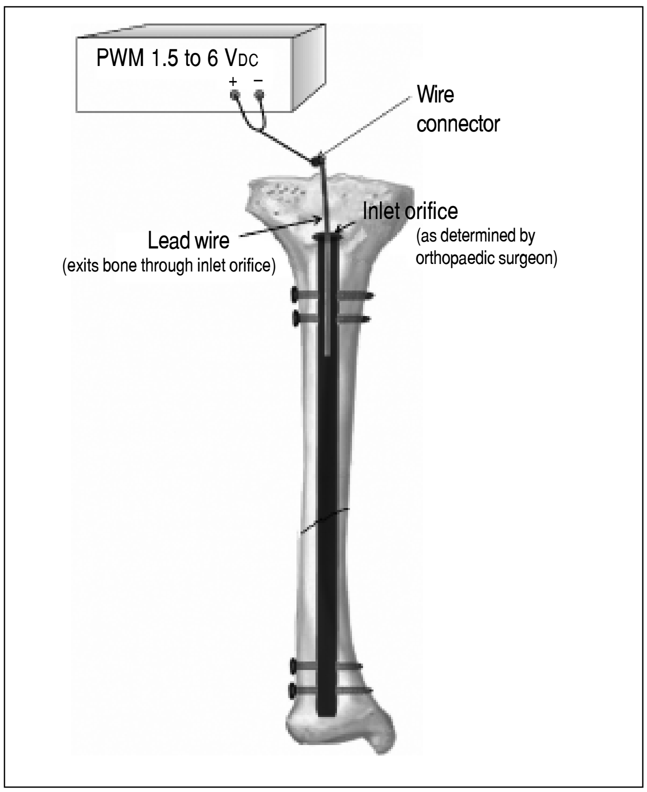

Figure 1. Active intramedullary nail.

Design and prototype fabrication

AutoDesk Inventor V 11 was used to design the active intramedullary nail. Five prototype active nails were manufactured of polished stainless steel 316LS, with two locking holes at each end. The proximal end was threaded to accommodate the insertion/extraction tool. Nails had a straight geometry in order to be able to perform future *in vivo* testing in sheep tibia. Outside diameter was 9.0 mm and internal, 7.0 mm. An electromechanical (7.0 x 31 mm) active element was manufactured on site. The device was energized from an external power sup-ply (Tektronix PS 280). This external power supply will be replaced by a self-contained power supply in the *in vivo* tests (figure 1 illustrates how the active intramedullary nail is stimulated).

Mechanical performance testing

Mechanical stimulation generated by the device was measured with a certified triaxial accelerometer (PCB Piezotronics, Triax mini 356A12) attached to the nail through one of the locking holes. A steel mounting block (14 x 14 mm external, r = 9.5 mm ID) was used to match the flat surface of the accelerometer with the round shape of the nail.

In vitro testing

An accelerated test was performed according to Reliasoft Corporation, Accelerated Life Testing Reference.[34]

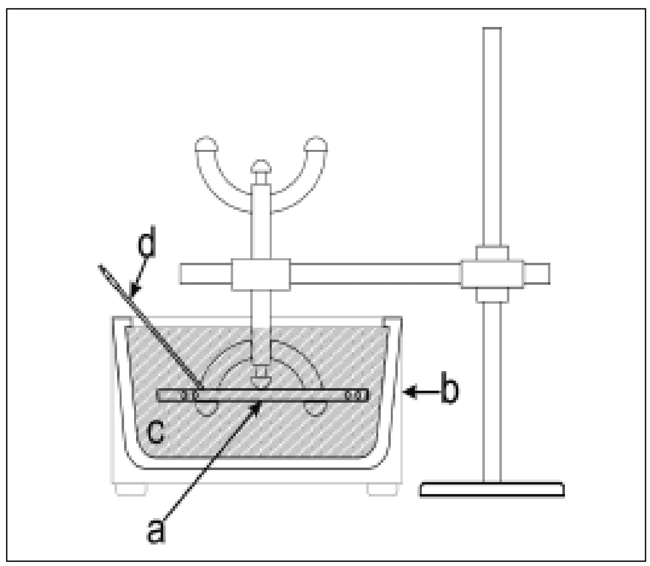

Figure 2. In vitro *testing apparatus.* ***a.*** *Active intramedullary nail.* ***b.*** *Recirculating bath.* ***c.*** *Physiologic solution.* ***d.*** *Lead wire.*

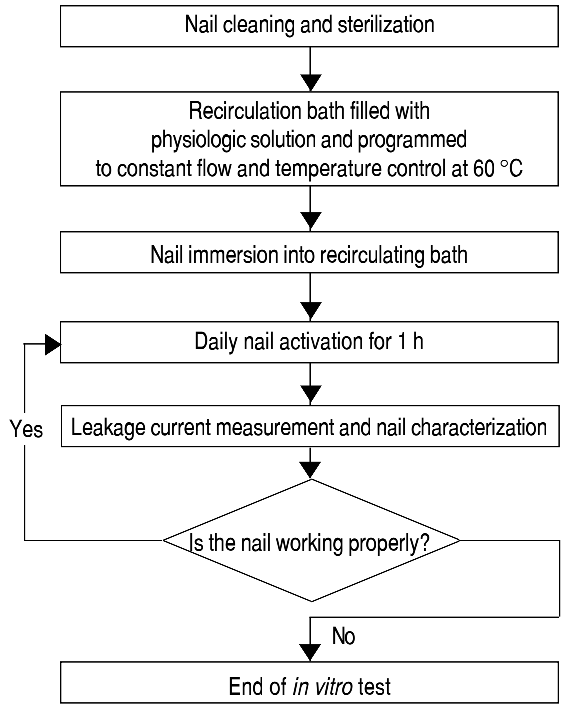

Figure 3. In vitro *testing procedure.*

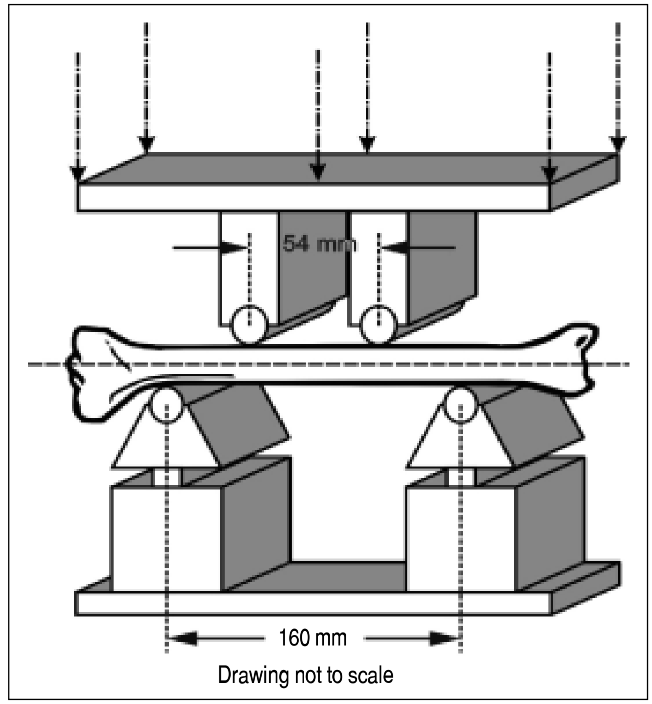

Figure 4. Active intramedullary nail mechanical testing apparatus.

Nails were tested *in vitro* utilizing a recirculating bath (Techne, Model 12/TE10A). Nails were tested for 14 days fully immersed in NaCl solution (0.9%) at 60 °C (Figure 2). Five days a week, the nails were taken out of the bath for a mechanical performance test as previously described. Then, the nail was reintroduced into the bath and turned on continuously for 20 min. Leakage current was measured continuously while the nail was turned on using a Dynatech Nevada 1000 Med Tester. After this period, the nail was again removed from the bath and a second mechanical performance test was performed. After the second measurement was concluded, nails were again placed in the saline solution bath for the following 24 h cycle. Saline was replaced every 24 h. Figure 3 illustrates the *in vitro* testing procedure.

Mechanical strength tests

Five active intramedullary nails were tested according to standard ASTM F 1264-03-A1.[28] As a comparison, three static nails of similar construction were also tested. To perform these tests, a universal testing machine (Instron Model 4502 Series IX) was employed. Testing procedure consists of setting the nail to be tested between two test supports and applying an incremental load at the center of the nail through two evenly spaced load rolls (Figure 4). According to the standard, the distance between test supports was 160 mm and the distance between load rolls was 50 mm.

Ex vivo experiments

One active intramedullary nail was tested *ex vivo* placing it sequentially in two adult sheep tibia (Suffolk, one year old male, 100 kg). In order to assess the full dynamic range of the active intramedullary nail it is important to take into account that in our design frequency and amplitude are dependent variables. Therefore to obtain full characterization of this particular active intramedullary nail three set of tests were performed:

- **Set 1.** Identify the frequency that results in minimum amplitudes (freq = 14.2 Hz, amplitudes: x = 300 mV, y = 1,200 mV and z = 1,100 mV).
- **Set 2.** Identify the frequency that produced maximum amplitudes (freq = 195 Hz, amplitudes: x = 780 mV, y = 2,960 mV and z = 2,960 mV).
- **Set 3.** Identify the amplitudes resulting at minimum frequency (freq = 11.4 Hz, amplitudes: x = 520 mV, y = 1,700 mV and z = 1,500 mV).

These values were specific to the nail tested and were measured with no-load and outside the bone.

Posteriorly, axial compression load to the tibias was applied using a universal testing machine (Instron Model 4502 Series IX). Axial load values applied independently to each tibia were 30, 60 and 100 kg. These values were selected considering that the animal weight was 100 kg and it could stand in four, two or one leg. Acceleration was measured using a certified triaxial accelerometer (PCB Piezotronics, Triax mini 356A12) attached to the proximal, medial and distal portions of the surface of the tibia shaft and averaging its values.

RESULTS

Design characteristics

The active nails complied with proposed geometry specifications including length, diameter, shape, threaded end, blocking orifices, and biocompatible materials.

Mechanical performance tests

The active nails are capable of producing an average (x, y, and z axes) acceleration force between 0.35 and 10.4 g. Acceleration is applied simultaneously by all three axes (Figure 5), resulting in axial and shear stimulation. The desired level of acceleration can be selected from a set of discrete values (Table 1). Acceleration levels are controlled externally. For each acceleration value, there is a limited number of frequencies that can be selected (Table 1).

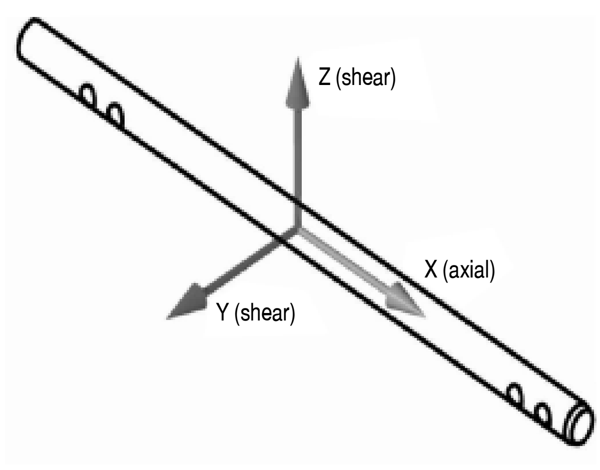

Figure 5. Axial and shear stimulation according to active nail axes.

Table 1. Active intramedullary nail minimum and maximum acceleration and frequency values.

	Frequency (Hz)	Acceleration (g)
Frequency (min)		
Axial	6.34* (0.01)	1.06 (0.05)
Shear	6.19* (0.05)	2.23 (0.13)
Frequency (max)		
Axial	172.05* (0.07)	8.17 (0.02)
Shear	172.13* (0.13)	10.46 (2.36)
Acceleration (min)		
Axial	29.82 (0.02)	0.35**(0.02)
Shear	29.68 (0.38)	0.44* *(0.05)
Acceleration (max)		
Axial	172.05 (0.07)	8.17** (0.02)
Shear	172.13 (0.13)	10.46** (2.36)

*Minimum or maximum value of frequency is attained only at the specified acceleration. **Minimum or maximum acceleration is attained only at the specified frequency.

In vitro tests

The new devices performed according to specifications throughout the entire *in vitro* testing period. The intramedullary nails complied with expected performance for an equivalent of 150 days. Leakage current was well below the standard for implantable devices (0.01 mA according to IEC 60601-1).[33] Visual and optical microscopy inspection revealed absence of surface corrosion including threaded section and locking holes.

Mechanical strength tests

After *in vitro* testing, the active nails were tested for mechanical resistance. All five prototypes exceeded the minimum load requirements according to standard ASTM F1264-03 Annex A1.[28] Static nails of similar geometry were used as controls. Figure 2 shows the results of the strength test.

Ex vivo experiments

Ex vivo experiments showed that acceleration magnitude decreased after inserting and securing the active intramedullary nail into the tibia. Posteriorly, an axial compression load of 30 kg, 60 kg, and 100 kg was applied to the experimental tibias, resulting in further attenuation of the acceleration magnitude. Results are shown on table 2. Acceleration values (g) were calculated for each axis, averaging the acceleration measured at distal,

Table 2. Axial and shear accelerations applied to the experimental bone by the active intramedullary nail.

		Active intramedullary nail with no bone & no load	Tibia 1			Tibia 2		
		Average (g)	Attenuation (%)	Applied to bone (g)	Equivalent (με)	Attenuation (%)	Applied to bone (g)	Equivalent (με)
Amp-min								
ampl 300 mV freq 14.2 Hz	x	0.9	32.06	0.62	10.29	41.67	0.53	8.84
ampl 1,200 mV freq 14.2 Hz	y	3.6	81.94	0.66	10.94	85.50	0.53	8.79
ampl 1,100 mV freq 14.2 Hz	z	3.3	71.26	0.96	15.97	79.59	0.68	11.34
Freq-min								
ampl 520 mV freq 11.4 Hz	x	1.6	51.47	0.76	12.74	56.03	0.69	11.55
ampl 1,700 mV freq 11.4 Hz	y	5.2	84.45	0.80	13.35	86.50	0.70	11.59
ampl 1,500 mV freq 11.4 Hz	z	4.5	70.90	1.32	22.05	79.70	0.92	15.38
Amp-max								
ampl 780 mV frec 195 Hz	x	2.36	31.73	1.61	26.89	52.74	1.12	18.62
ampl 2,960 mV frec 195 Hz	y	8.97	79.93	1.80	30.01	81.80	1.63	27.21
ampl 2,960 mV frec 197 Hz	z	8.97	74.49	2.29	38.13	82.39	1.58	26.33

medial and proximal sections at the surface of the tibial shaft.

DISCUSSION

Multiple authors have suggested that the mechanical environment and timing influence the pattern of fracture healing.[1,15,30,35,36] External fixators have been used to study the dynamics of fracture healing, either by applying external movement and loads[1,37,38] or by indirectly measuring fracture stiffness (rate of fracture healing) through interfragmentary movement.[1,39]

Reports utilizing external fixators describe experiments in different species, devices with different mechanical properties, and a wide variety of measured parameters regarding bone healing and other variables, all of which render it difficult to compare results and determine the ideal characteristics that a mechanical stimulation device should possess in order to accelerate bone healing.

On the other hand, Fritton, *et al.* (2000)[40] measured *in vivo* the strain history experienced througout 12 or 24 h of normal activity from the tibia of an adult male dog, a male turkey, an ewe, and from the ulna of three adult male turkeys. The authors were able to identify that the highest magnitude strains (2,000-3,000 $\mu\varepsilon$) occur only a relatively few times a day, while very small strains (< 10 $\mu\varepsilon$) take place thousands of times daily.

Using this strategy (inducing small magnitude strains at high frequency), Hwang, *et al.*[29] experimented applying oscillatory accelerations to scaffolded and non-scaffolded calvarial defects in rats, and reported that low-level, high-frequency (0.4 g and 45 Hz) accelerations can enhance bone healing in both groups. Also, Goodship, *et al.* 2009[41] was able to increase bone mineral content significantly (by 52%) when applying stimulation of extremely low magnitude (25 $\mu\varepsilon$) and high frequency (30 Hz).

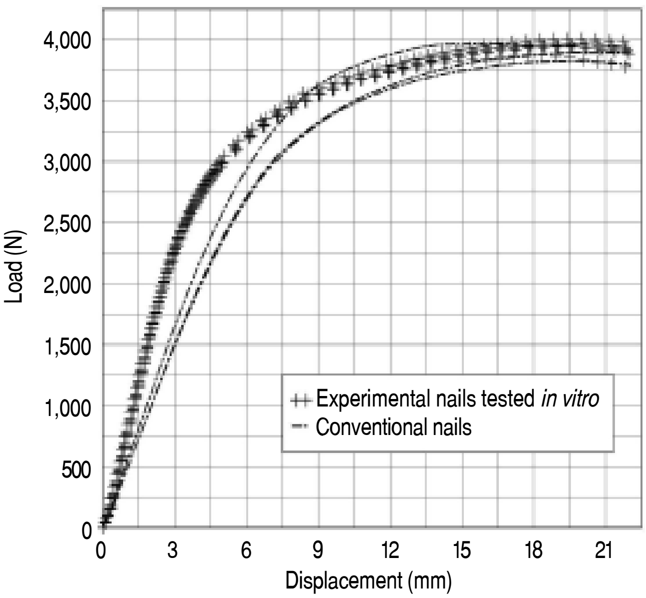

Figure 6. Active nail mechanical strength test.

Given that it is intrinsically difficult to assess the magnitude and direction of the mechanical stimulus that is being applied to the fracture through an external fixator, an intramedullary active nail was designed and fabricated considering the elimination of the disadvantages of external fixators, and addition of the benefits of intramedullary nailing.

This novel device complies with the proposed design parameters and the requirements for implantable devices such as materials, geometry, insertion/extraction port, locking holes, and mechanical strength according to standards. These characteristics will allow future *in vivo* experimentation applying different frequencies and their associated acceleration values throughout different time intervals and during different times of initial stimulation.

The previously described prototype performs mechanically with or without the active element. This feature ensures that in worst case scenarios, in which the active element fails on being tested *in vivo,* the mechanical structure of the intramedullary nail will act as a standard intramedullary nail that will allow bone healing to continue without needing to replace the intramedullary nail, as illustrated in figure 6. However, torsion tests according to standard [ASTM F1264 -03 part A2 (Test method for static torsional testing of intramedullary fixation devices)][28] must be conducted to truly assess its complete mechanical behavior.

The designed active nail has two limitations. One is that frequency and acceleration values are interdependent; each frequency only permitting up to four different levels of acceleration. That is, each acceleration level allows for two different frequencies. This limitation is imposed by the design of the active element. However, the range of acceleration and frequency values of which the device is capable of delivering provides an ample platform to perform bone healing experiments using low-magnitude, high-frequency stimulation.

The second limitation is that the active nail will generate axial and shear accelerations simultaneously, both dependent of selected frequency. Axial and shear accelerations are of different magnitudes. These magnitudes are also interdependent and are intrinsic to the design of the active element.

Ex vivo experiments showed that acceleration attenuation occurs when mass increases (inserting the active intramedullary nail into the bone) and also, when load is applied to the bone. These results were expected according to Newton's second law. On the other hand, for a given set of stimulating parameters (frequency and amplitude as described in table 1), acceleration values, measured on the surface of the bone, changed along the tibial shaft possibly due to the non-uniform anatomical structure of the bone and its interaction with the active intramedullary nail. However, the technical characteristics of the active intramedullary nail allow for acceleration and frequency compensation through the selection of a different set of stimulation parameters.

Prototype performance exceeded expected useful life. The device lasted an equivalent of 150 days (accelerated tests). *In vivo* tests will require 15-21 active days.[1,9,12] During the remaining time, the active nail should perform as a static nail.

Another advantage is that the active nail appears to be and handles like a standard static nail. This will allow rapid integration of this technology into standard orthopedic surgery practice. No additional specialized training would be required. Surgical time will remain unchanged because active nail blocking will be achieved with standard guides and fluoroscopic navigation.

Rubin,[31] measuring acceleration *in vivo,* on sheep tibia, established that an acceleration of 0.3 g induced a 5 $\mu\varepsilon$ on the surface of the live tibia. Using this data, the active intramedullary nail used in the *ex vivo* experiment, would apply the following strains to tibia 1 and 2 as shown in table 3. This level of mechanical stimulation, according to Fritton,[40] occurs naturally several thousands of times a day in healthy bone. Also, Rubin[31] reported that this mag-

Table 3. Strain (με) induced in tibia 1 and 2 by the experimental active intramedullary nail.

	Tibia 1				Tibia 2			
Axis	Amp-min f = 14.2 Hz		Amp-max f = 195 Hz		Amp-min f = 14.2 Hz		Amp-max f =195 Hz	
x	10.29	με	26.89	με	8.34	με	18.62	με
y	10.94	με	30.01	με	8.79	με	27.21	με
z	15.97	με	38.13	με	11.34	με	26.33	με

nitude of stimulation, when applied externally 20 min/day, induces significant increase in bone mineral density in intact bone.

Also, when a fracture occurs, the normal array of mechanical stimulus that are applied to healthy bone during regular activities is reduced markedly, and the degree to which this array of mechanical stimulus would be reestablished to the bone will be largely influenced by the method of fracture fixation. Therefore, the active intramedullary nail may enhance bone healing by providing an array of mechanical stimulus to the fracture site not provided by traditional fracture fixation methods.

The authors acknowledge that additional experiments are required in order to statistically validate the strain that can be induced *in vivo* by the active intramedullary nail. Furthermore, *in vivo* experiments using simple fractures of the tibial shaft need to be conducted in order to assess if effectively, applying active mechanical stimulation *in situ* enhances bone healing.

For the patient, successful active nailing offers the potential of faster return to work and/or activities of daily living. Also, active nailing entertains the potential of cost reduction by achieving better bone quality in the same or in a reduced amount of time.

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