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Biomechanics and Surface Activity in Simulated Body Fluid of Antibiotic Intramedullary Nail

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ABSTRACT

Intramedullary nail continues to evolve with the introduction of new technologies as it is considered a gold standard in treating bone defects caused by disease, trauma and accidents which are evidently higher in developing countries like the Philippines. Recently, Philippine Orthopedic Center introduced the usage of Antibiotic Intramedullary Nails (ABIMN), a threaded stainless rod coated with antibiotic cement to treat infections that commonly occurs in bone defects. The product has been widely used, however, no biomechanical study was made to demonstrate and test the coronal bending, cyclic axial loading and chemical properties of the ABIMN. The researchers compared the biomechanical properties and surface activity when immersed in Simulated Body Fluid (SBF) of the Antibiotic Intramedullary Nail (ABIMN), Küntscher Intramedullary Nail (KIMN), and Intramedullary Nail with Interlocking screws (IMNIS). A total of 37 Intramedullary Nail (IMN) models were used for the biomechanical study, while the 4 remaining nails were used for the SBF immersion test. A very high positive correlation between bending rigidity and radius to the 4th power in ABIMN was found. Median Young's modulus of elasticity on the other hand, significantly differs across the three groups. Further analysis showed that the median value was significantly lower in ABIMN compared to KIMN ($p=0.0027$) and IMNIS ($p=0.0025$) concluding that the ABIMN can be left for 6 weeks, with the patient on partial weight bearing up to 25% of an average 75kg man. The chemical properties of the ABIMN however, revealed that it is safe to use and has qualitatively comparable corrosion properties of KIMN when immersed in SBF. For easier removal of the ABIMN and after completion of both oral and IV antibiotics at 6 weeks post op; it still advisable to remove the ABIMN and perform exchange nailing at the said timeframe.

Key words: Antibiotic Intramedullary Nail (ABIMN), Küntscher Intramedullary Nail (KIMN), Biomechanics, Osteomyelitis, Simulated Body Fluid (SBF)

1. INTRODUCTION

The World Health Organization (WHO) reported in 2018 that road accident was the 8th leading cause of death globally wherein, countries from Southeast Asia contributed a higher rate than other areas at 20.7 deaths per 100,000 populations [1]. As the trend projects that this will continue in the foreseeable future, the Philippines, one of the developing countries in South East Asia, already considered road accident a major concern when an approximate 7,000 deaths were reported last 2017 and also a large number were figured as orthopedic trauma patients [2]. The challenge is that inadequate care from these patients could also lead to higher mortality rate as various orthopedic infections occurs frequently from these defects.

Orthopedic Infections and osteomyelitis remain challenging case to treat since bone provides a unique environment for bacteria to grow, with low vascularity and low turnover rate [3]. Osteomyelitis can be classified according to duration, (acute, chronic), pathogenesis (trauma, contiguous spread, hematogenous, surgical), site, extent, or type of patient [4]. The Cierny-Mader classification is a clinical classification based on anatomic, clinical, and radiologic features. It characterizes osteomyelitis as being in one of four anatomic stages. Stage 1, or medullary, osteomyelitis is confined to the medullary cavity of the bone. Stage 2, or superficial, osteomyelitis involves only the cortical bone and most often originates from a direct inoculation or a contiguous focus infection. Stage 3, or localized, osteomyelitis usually involves both cortical and medullary bone. In this stage, the bone remains stable, and the infectious process does not involve the entire bone diameter. Stage 4, or diffuse, osteomyelitis involves the entire thickness of the bone, with loss of stability, as in infected nonunion. The Cierny-Mader system adds a second dimension, characterizing the host as either A, B, or C. The A hosts are patients without systemic or local compromising factors. B hosts are affected by one or more compromising factors. C hosts are patients so severely compromised that the radical treatment necessary would have an unacceptable risk-benefit ratio. Osteomyelitis is treated both with antibiotics and surgery depending on stage of infection.The Philippine Orthopedic Center addressed this concern when they developed the Antibiotic Intramedullary Nail (ABIMN), a threaded stainless rod coated with antibiotic cement to treat infections that commonly occurs in bone defects.

Following the principle behind antibiotic cement-coated interlocking intramedullary nails that often used vancomycin, tobramycin, and gentamicin as antibiotics. [5-8].

Antibiotic therapy may be directed with regard to the stage of the infection. In adults, a stage 1 infection is more refractory to therapy and usually is treated with both antibiotics and surgery. With stage 2 infections, the patient may be treated with a 2-week course of antibiotics after superficial debridement and soft tissue coverage. In these cases, the arrest rate is 80%. In stages 3 and 4, the patient is treated with 4 to 6 weeks of antimicrobial therapy dated from the last major debridement. At this stage of the disease, most antibiotic regimens will fail without adequate debridement regardless of the duration of therapy.

Antibiotic-impregnated acrylic beads or antibiotic-loaded cement also may be used to sterilize and temporarily maintain dead space [5-7]. The beads are usually removed after 2 to 4 weeks and replaced with a cancellous graft. The antibiotics used in the beads are most often vancomycin, tobramycin, and gentamicin [8]. Chronic osteomyelitis of bone with nonunion or bone defects is traditionally treated by a two-stage procedure involving initial debridement and antibiotic delivery, with initial external fixation, and then definitive internal fixation. Antibiotic cement-coated interlocking intramedullary nails can help convert two-stage processes into a single-stage procedure and can be used in patients who are not ideal candidates for external fixation, as well as in patients who do not want to have an external fixator applied [9-11].

Despite the widespread use of the antibiotic intramedullary nail for osteomyelitis and as for a bridge from external fixation to definitive intramedullary fixation, no biomechanical study was made to demonstrate and test the coronal bending, cyclic axial loading and chemical properties of the said intramedullary nails.

This study aims to define the biomechanical properties of the Antibiotic Intramedullary Nail (ABIMN) in terms of coronal bending or four-point bending, cyclic axial compression loading or fatigue and chemical properties; and compare it with the biomechanical properties of a Küntscher Intramedullary Nail (KIMN) and an Intramedullary Nail with Interlocking Screws (IMNIS). In addition, this study could also show if a thicker diameter cement coating of an ABIMN is significantly stronger than a thinner diameter cement coating of an ABIMN, and if the bending rigidity of the ABIMN is proportional to its radius to the 4th power.

This would also define the advantages and disadvantages of the ABIMN terms of early weight bearing and rehabilitation post operation. Permitting weight bearing and adjacent joint range of motion during the early post-operative period will lessen the chances of disuse osteopenia and joint contracture that could complicate the definitive surgery. In addition, this study would also describe the chemical composition through x-ray fluorescence and corrosive properties after chemical immersion of the widely used antibiotic nail in the Philippines for chronic osteomyelitis.

2. MATERIALS AND METHODS

The researchers employed an experimental study to compare the biomechanical properties and a simulation analysis of ABIMN, KIMN, and IMNIS. The study was conducted at Department of Science and Technology - Metals Industry Research and Development Center (DOST - MIRDC), Gen. Santos Ave., Bicutan, Taguig City, 1631 Metro Manila, Philippines.

This would explain the minimum number of samples per subgroup. A total of 41 intramedullary models, three of each group implant construct of antibiotic intramedullary nail; three of each group implant construct of Küntscher intramedullary nail and one of each implant construct of intramedullary nail of the femur and tibia. This was based on previous biomechanical studies done, that three (3) IMNs per subgroup would suffice. [15] A total of 37 intramedullary nail models were used for the biomechanical study, while the 4 remaining were used for the immersion test in Simulated Body Fluid (SBF).

2.1 Intramedullary Nails

2.1.1 Antibiotic Intramedullary Nail

Figure 1 shows on how the Antibiotic Intramedullary Nail was prepared. Seventeen (17) nails with 330 mm length and diameters 10, 12 and 13 mm were achieved by setting a 400mm x 4mm threaded rod into the ABIMN mold, with one nut distally and one nut proximally along with a stopper outside the mold to make a 330mm ABIMN (longest length possible). Generous amount of KY jelly is applied along the entire length of the mold. One (1) pack of plain bone cement was mixed with four (4) grams of vancomycin into a mixing bowl and packed in placed by hand into both sides of the mold. The mold is closed, then a mallet is used to pound the mold to evenly distribute the bone cement into the entire length of the mold, and a rubber tubing is wrapped around the mold and finally secured with Kocher forceps. The mold is again pounded using a mallet. After setting, the mold is opened, excess bone cement is removed using a osteotome, and the threaded rod is then hammered out of the mold through sliding onto the proximal side. The ABIMN is then carefully lifted out the mold. Edges of the ABIMN are sanded off using a bone file and excess of the threaded rod is cut using a rod cutter or a Berbecker.

2.1.2 Küntscher Intramedullary Nail (KIMN)

Seven (7) 440mm x 10mm and six (6) 440mm x 11mm were purchased from Olten Instruments, Pakistan and Czech Implants, Czech Republic, respectively.

2.1.3 Intramedullary Nail with Interlocking Screws (IMNIS)

Two (2) 380mm x 10mm, one (1) 10mm x 400mm, one (1) 10mm x 420mm for the femur, two (2) 360mm x 10mm for the tibia were purchased from Smith & Nephew, England.

2.2 Mechanical Testing

2.2.1 Coronal Bending

Specimens were loaded on the compression testing machine (Zwick Roell 10kN) by means of steel cylindrical supports, which were adjusted equidistant to the vertical machine axis. 4-point loading was conducted at a speed of 10mm per minute between 25 and 250N, with load and displacement data acquisition at a frequency of 10Hz. This was measured in Newtons.

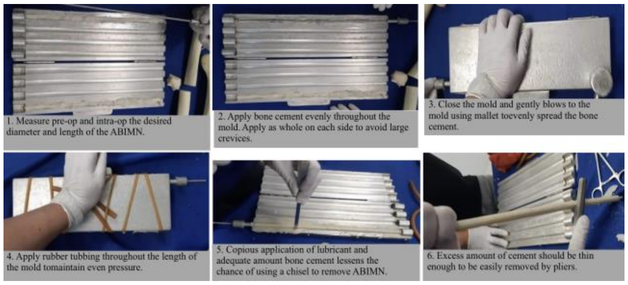
Since the ABIMN is made of two different materials, data were collected when there was visible deformation and breaking of the bone cement coat and when there was visible deformation of the inner rod (fracture stress level and ultimate tensile stress). For KIMN and IMNIS data were collected when there was a visible deformation (fracture stress) of the said nails [12].

2.2.2 Cyclic Axial Loading

Specimens were loaded on fatigue testing machine (Zwick Roell 1 kN) by means of steel jigs fitted at the proximal and distal ends of the intramedullary nails. Loading was started at 300N to 1800N with a loading increment of 100N at 1Hz for 100 cycles, allowing 10 sec. rest between each load increment [13].In this setup, applied loads represent one to two- fold body weight of an average 65 to 85 kg., equivalent to 6 weeks of full weight bearing throughout the gait cycle [14,15]. For ABIMN, KIMN and IMNIS data will be collected when there is visible breakage of the said nails.

2.3 Chemical and SBF Immersion Test

Each implant was verified and underwent chemical testing using X-ray Fluorescence Spectrometer (XRF), Thermo Niton, XL3t GOLDD+, to reveal the composition of each IMN and compare them to each other. All nails were cut at approximately 10 mm length using power hacksaw, cleaned using acetone and air-dried prior to analysis. The instrument was operated using the pre-set General Metals mode which has 3 filters that can trace 31 elements ranging from Magnesium to Bismuth, pre-built calibration database for element quantification and material identification of the commonly analyzed alloys. Each sample was bombarded through the X-ray tube (50kV, 200µA, for 30 seconds count) and was repeated 5 times at different location points. Accuracy of measurements was regularly tested using Certified Reference Materials SS 465/1 and 466/1 (British Chemical Standard, MBH Analytical Ltd.). Accuracy of IMNIS was not checked as there was no similar reference material available during the conduct of analysis [16].



1. Measure pre-op and intra-op the desired diameter and length of the ABIMN.

2. Apply bone cement evenly throughout the mold. Apply as whole on each side to avoid large crevices.

3. Close the mold and gently blows to the mold using mallet toevenly spread the bone cement.

4. Apply rubber tubbing throughout the length of the mold tomaintain even pressure.

5. Copious application of lubricant and adequate amount bone cement lessens the chance of using a chisel to remove ABIMN.

6. Excess amount of cement should be thin enough to be easily removed by pliers.

Figure 1: Molding the Antibiotic Intramedullary Nail

The IMNs also underwent immersion testing in Simulated Body Fluid (SBF) at pH 7.4 which represented the synovial fluid pH or the pH at which bone mineralization peaks [17, 18]. The samples were cleaned with acetone and distilled water for several times and then air dried. Samples are then placed in a dessicator for 24 hours before the conduct of the immersion testing. A simulated body fluid (SBF) was prepared similar to the studies made by Kokubo et al. and Fan Xin et al. [19-21]. The pH of the prepared solution was then adjusted at 7.4 at 37.0 degrees Celsius using hydrochloric acid and tris-(hydroxymethyl)-aminomethane similar to the synovial fluid and blood plasma [17,18]. Each of the samples were immersed in a flask, sealed and placed under constant temperature of 37.0 degrees Celsius using a water bath for 30 days. Specimens were then rinsed with distilled water, acetone and oven-dried at 40 degrees Celsius for 2 hours. The pH level was determined for the first, seventh, twenty first and thirtieth day using a pH meter (InoLab 720). Surface morphology on the other hand was evaluated using a Scanning Electron Microscope (Hitachi SU3500). This revealed what each implant generated as corrosion products and described each implant's surface morphology after a pre-determined period of time.

2.4 Data Analysis

Data were encoded in MS Excel by the researchers. Stata MP version 16 software was used for data processing and analysis. Continuous data were presented as mean / standard deviation (SD) or median / interquartile range (IQR) depending on data distribution. The assumptions of ANOVA including normality and homogeneity of variance were assessed before the analyses. If assumptions were met, One Way ANOVA was used to compare the values across groups. Otherwise, the non-parametric Kruskal Walls (KW) test was performed. Significant KW-test were further analyzed using Dunn's test. P values ≤0.05 were considered statistically significant.

3. RESULTS

3.1 Biomechanical Properties

3.1.1 Coronal Bending

A total of 18 intramedullary nails underwent four point bending testing. One (1) sample of ABIMN 11mm x 330mm and one (1) sample of KIMN 11mm x 440mm were deemed damaged and bent prior to testing and were both excluded from the study. Table 1 shows the median values during coronal bending by type of intramedullary nails. The researcher did not use ANOVA since the data violates two assumptions, normality and homogeneity of variance based on the preliminary examination of data. Thus, the non-parametric alternative Kruskal Wallis test was used. This test compares the median instead of the mean

Median four point bending loads significantly differ across the three groups (Table 1). Further analysis (Table 2) showed that the median four point bending load was significantly lower in ABIMN compared to KIMN (p=0.0027) and IMNIS (p=0.0025).

Median deflection at bending load significantly differ across the three groups (Table 1). Further analysis (Table 3) showed that the median deflection at bending load was significantly lower in ABIMN compared to KIMN (p=0.0008) and IMNIS (p=0.0204) (Table 3).

Median Young's modulus of elasticity significantly differ across the three groups. Further analysis showed (Table 4) that the median value was significantly lower in ABIMN compared to KIMN (p=0.0027) and IMNIS (p=0.0025). There is no significant difference in the median four point bending load, median deflection at bending load and median Young's modulus of elasticity between KIMN and IMNIS (p=0.2166, p=0.4342, p-0.2166)

Table 1: Median load values during coronal bending by type of intramedullary nails (n=18)

	ABIMN (n=11) Median [IQR]	**KIMN (n=5) Median [IQR]**	**IMNIS (n=2) Median [IQR]**	**P VALUE[a]**
Four point bending load (N)	436.36 [390.10-472.99]	1498.35 [1341.11-1722.84]	4398.26 [4273.73-4522.79]	0.0017*
Deflection at bending load (mm)	12.38 [9.71-15.54]	25.94 [25.70-29.01]	26.49 [22.74-30.25]	0.0029*
Young's modulus of elasticity	41.98 [32.67-49.90]	222.16 [204-88-268.41]	369.07 [366.87-371.26]	0.0017*

[a] Kruskal Wallis test was used; significant results were further analyzed using Dunn's test

Table 2: Posthoc Comparison Using Dunn's Test of Load Values During Coronal Bending - Four Point Bending

	ABIMN	**KIMN**
KIMN	0.0027*	-
IMNIS	0.0025*	0.2166

p values of pairwise comparisons are presented;
*denotes significant difference at the 0.05 level

Table 3: Posthoc Comparison Using Dunn's Test of Load Values During Coronal Bending - Deflection at Bending Load

	ABIMN	**KIMN**
KIMN	0.0008*	-
IMNIS	0.0204*	0.4342

p values of pairwise comparisons are presented;
*denotes significant difference at the 0.05 level

p values of denotes significant difference at the 0.05 level

Table 4: Posthoc Comparison Using Dunn's Test of Load Values During Coronal Bending - Young's Modulus of Elasticity

	ABIMN	KIMN
KIMN	0.0027*	-
IMNIS	0.0025*	0.2166

p values of pairwise comparisons are presented;
*denotes significant difference at the 0.05 level

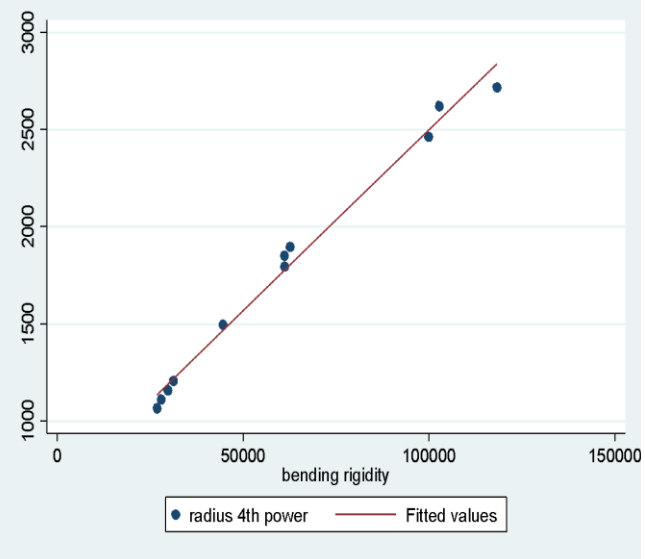


Figure 2: Correlation of Bending Rigidity and Radius to the 4th Power in ABIMN (n=11)

Figure 2 shows that there is a very high positive correlation between bending rigidity and radius to the 4th power in ABIMN nails (r=0.9941, p value<0.00001).

Table 5 shows the median stiffness values during coronal bending by type and diameter of intramedullary nails. Only the ABIMN underwent the Four Point Maximum Bending Load testing, since the ABIMN is composed of two different materials. Noted increase in the four point maximum bending load from the four point bending load.

Table 5: Median Loads Values During Coronal Bending by Type and Diameter of Intramedullary Nails (n=18)

	Median [IQR]							P VALUE^a
	ABIMN 10 (n=3)	ABIMN 11 (n=2)	ABIMN 12 (n=3)	ABIMN 13 (n=3)	KIMN 10 (n=3)	KIMN 11 (n=2)	IMNIS 10 (n=2)	
Four point bending load (N)	439.36 [420.27-441.75]	378.78 [348.14-409.41]	454.19[245.15-472.99]	485.62[390.10-6078.66]	1341.11[1333.03-1498.35]	1733.56[1722.84-1744.28]	4398.26[4273.73-4522.79]	0.0287*
Deflection at bending load (mm)	15.57 [15.54-17.69]	10.35[10.35-10.35]	12.20[6.03-12.57]	9.71[8.44-13.28]	25.70[25-25.94]	29.66[29.01-30.31]	26.49[22.74-30.25]	0.0277*
Four Point Maximum Bending Load (Nmax)	440.76 [422.25-505.64]	431.08 [428.36-433.80]	563.26[538.09-596.70]	625.87[615.56-797.36]	-	-	-	0.0320*
Young's modulus of elasticity	31.99 [31.96-32.67]	35.39 [32.90-37.88]	42.01[41.98-43.33]	51.62[49.90-55.41]	204.8[184.68-222.16]	313.9[268.41-359.39]	369.0[366.87-371.26]	0.0106*

^{a}Kruskal Wallis test was used; significant results were further analyzed using Dunn's Test
- only the ABIMN underwent Four Point Maximum Bending Load Testing

3.1.2 Four Point Bending Load

Median four point bending load significantly differ across groups (Table 5). Further analysis (Table 6) showed that the median four point bending load of ABIMN 10 was significantly lower compared to KIMN 11 (p=0.0256) and IMNIS 10 (p=0.0091), but not with other types (all p's>0.05). Median four point bending load of ABIMN 11 was significantly lower compared to KIMN 10 (p=0.0201), KIMN 11 (p=0.0096) and IMNIS 10 (p=0.0033), but not with other types (all p's>0.05). Median four point bending load of ABIMN 12 was significantly lower compared to KIMN 11 (p=0.0256) and IMNIS 10 (p=0.0091), but not with other types (all p's>0.05). Median four point bending load of ABIMN 13 was significantly lower compared to IMNIS 10 (p=0.0256), but not with other types (all p's>0.05).

No significant difference between KIMN 10 and 11 (p=0.3040) and between IMNIS and KIMN 10 (p=0.1779) and 11 (p=0.3540).

3.1.3 Deflection at Bending Load

Median deflection at bending load significantly differ across groups (Table 5) and further analysis (Table 7) showed that the median deflection at bending load of ABIMN 10 does not significantly differ with other types (all p's>0.05). Median deflection at bending load of ABIMN 11 was significantly lower compared to KIMN 11 (p=0.0262), but not with other types (all p's>0.05). Median deflection at bending load of ABIMN 12 was significantly lower compared to KIMN 10 (p=0.0145), KIMN 11 (p=0.0046) and IMNIS 10 (p=0.0197), but not with other types (all p's>0.05). Median deflection at bending load of ABIMN 13 was significantly lower compared to KIMN 10 (p=0.0145), KIMN 11 (p=0.0046) and IMNIS 10 (p=0.0197), but not with other types (all p's>0.05).

No significant difference between KIMN 10 and 11 (p=0.2576) and between IMNIS and KIMN 10 (p=0.4568) and 11 (p=0.3103).

3.1.4 Four Point Maximum Bending Load

Median Four Point Maximum Bending Load was only performed for ABIMN and was significantly different across the four groups (Table 5). Further analysis (Table 8) showed that the median value of ABIMN 10 and ABIMN 11 were significantly lower compared to ABIMN 13 (p=0.0069, p=0.0066), not with other types (all p's>0.05).

No significant difference between ABIMN 12 and 13 (p=0.1340).

Table 6: Posthoc Comparison Using Dunn's Test of Median Load Values During Coronal Bending - Four Point Bending Load

	ABIMN 11	**ABIMN 12**	**ABIMN 13**	**KIMN 10**	**KIMN 11**	**IMNIS 10**
ABIMN 10	0.2691	0.5000	0.3232	0.0541	0.0256*	0.0091*
ABIMN 11	-	0.2691	0.1525	0.0201	0.0096*	0.0033*
ABIMN 12	-	-	0.3232	0.0541	0.0256*	0.0091*
ABIMN 13	-	-	-	0.1257	0.0619	0.0256*
KIMN 10	-	-	-	-	0.3040	0.1779
KIMN 11	-	-	-	-	-	0.3540

p values of pairwise comparisons are presented; *denotes significant difference at the 0.05 level

Table 7: Posthoc Comparison Using Dunn's Test of Median Load Values of Deflection at Bending Load

	ABIMN 10	ABIMN 11	ABIMN 12	ABIMN 13	KIMN 10	KIMN 11
ABIMN 11	0.1956	-	-	-	-	-
ABIMN 12	0.1126	0.5000	-	-	-	-
ABIMN 13	0.1126	0.5000	0.5000	-	-	-
KIMN 10	0.1660	0.0614	0.0145*	0.0145*	-	-
KIMN 11	0.0644	0.0262*	0.0046*	0.0046*	0.2576	-
IMNIS 10	0.1645	0.0623	0.0197*	0.0197	0.4568	0.3103

p values of pairwise comparisons are presented; *denotes significant difference at the 0.05 level

Table 8: Posthoc Comparison Using Dunn's Test of Median Load Values During Coronal Bending - Four Point Maximum Bending Load

	ABIMN 10	ABIMN 11	ABIMN 12
ABIMN 11	0.3916	-	-
ABIMN 12	0.0879	0.0686	-
ABIMN 13	0.0069*	0.0066*	0.1340

p values of pairwise comparisons are presented; *denotes significant difference at the 0.05 level

3.1.5 Young's Modulus of Elasticity

Median Young's modulus of elasticity significantly differ across groups (Table 5). Further analysis (Table 9) showed that the median value of ABIMN 10 was significantly lower compared to ABIMN 13 (p=0.0332), KIMN 10 (p=0.0058), KIMN 11 (p=0.0028) and IMNIS 10 (p=0.0007) but not with other types (all p's>0.05). Median value of ABIMN 11 was significantly lower compared to KIMN 10 (p=0.0406), KIMN 11 (p=0.0197) and IMNIS 10 (p=0.0074) but not with other types (all p's>0.05). Median value of ABIMN 12 was significantly lower compared to KIMN 11 (p=0.0406) and IMNIS 10 (p=0.0156) but not with other types (all p's>0.05). Median value of ABIMN 13 does not significantly differ with KIMN 10, KIMN 11 and IMNIS 10 (all p's>0.05). Median value of KIMN 10 does not significantly differ with KIMN 11 and IMNIS 10 (all p's>0.05).

No significant difference between IMNIS and KIMN 11 (p=0.3540).

Table 9: Posthoc Comparison Using Dunn's Test of Median Values of Young's Modulus of Elasticity

	ABIMN 10	ABIMN 11	ABIMN 12	ABIMN 13	KIMN 10	KIMN 11
ABIMN 11	0.30	-	-	-	-	-
ABIMN 12	0.12	0.30	-	-	-	-
ABIMN 13	0.033*	0.13	0.25	-	-	-
KIMN 10	0.0058*	0.041*	0.0843	0.25	-	-
KIMN 11	0.0028*	0.020*	0.0406*	0.13	0.30	-
IMNIS 10	0.0007*	0.0074*	0.0156*	0.062	0.18	0.35

p values of pairwise comparisons are presented; *denotes significant difference at the 0.05 level

3.1.6 Cyclic Axial Loading

A total of 17 intramedullary nails underwent cyclic compression testing. Table 6 shows the mean stiffness values during cyclic axial compression by type of intramedullary nails.

Tables 10 and 11 both show that there is no significant difference in the mean stiffness values across the groups.

Table 10: Mean load values during cyclic axial compression by type of intramedullary nails (n=17)

	ABIMN (n=9) Mean ± SD	KIMN (n=6) Mean ± SD	IMNIS (n=2) Mean ± SD	P VALUE[a]
Axial Cyclic Loading, Breaking Load (N)	1034.78 ± 650.29	1562.33 ± 362.24	1413 ± 547.30	0.2190

[a]One way ANOVA was used

-No significant difference in the mean stiffness values during cyclic axial compress across groups

Table 11: Mean load values during cyclic axial compression by type and diameter of intramedullary nails (n=17)

	ABIMN 10 (n=3)	ABIMN 11 (n=3)	ABIMN 12 (n=3)	KIMN 10 (n=3)	KIMN 11 (n=3)	IMNIS 10 (n=2)	P VALUE
Axial Cyclic Loading, Breaking Load (N)	943.33 ± 714.63	915 ± 589.16	1246 ± 856.01	1533 ± 400.84	1591.67 ± 405.96	1413 ± 547.30	0.6545

No significant difference in the mean stiffness values during cyclic axial compress across groups

Table 12: X-ray Fluorescence Testing

	Silicon	Chromium	Manganese	Iron	Nickel	Copper	Molybdenum	Cobalt	Aluminum	Titanium	Vanadium	Metal Identification
ABIMN	0.777	18.58	1.21	70.82	7.56	0.456	0.240	-	-	-	-	Stainless Steel 304
KIMN	0.545	16.72	1.32	69.17	9.37	0.84	1.95	0.413	-	-	-	StainlessSteel 316
IMNIS	0.261	-	-	0.322	0.045	-	-	-	4.91	89.92	4.64	Titanium6-4

3.2 Immersion in Simulated Body Fluid

The chemical composition of the nails was verified first prior to immersion testing using a Portable X-ray Fluorescence Spectrometer (XRF). The 10, 12 and 13 mm ABIMN has shown notable Chromium and Nickel content at approx. 18% and 7% (w/w), respectively which makes it a stainless steel material. But due to low Molybdenum content, the ABIMN was identified as Stainless Steel Grade 304 (SS 304) [22].

The KIMN was also identified as Stainless Steel from XRF analysis due to high concentrations of Nickel and Chromium at 9.37% and 16.72%, respectively. The high Molybdenum content at 1.95% however, was different from that of ABIMN and was assessed as Stainless Steel Grade 316 material [22].

The EDXRF alloy database identified the IMNIS nail as Ti 6Al-4V or a Grade 5 Titanium Alloy that exhibits high tensile strength and corrosion resistance which is well-suited for surgical implants like intramedullary nails [23]. The chemical testing results was summarized in Table 12.

Figure 3 and Table 13 shows the changes in pH of the SBF solution during the immersion of IMNs samples.

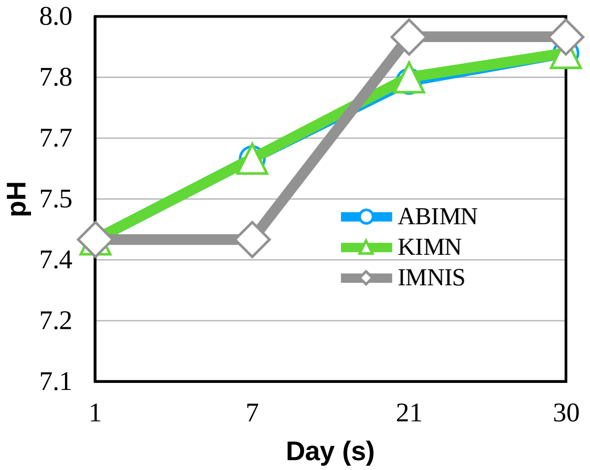


Figure 3: Change in pH of the SBF Solution

Table 13: Summary of the Change in pH of the SBF Solution for the Different IMNs

Day (s)	pH Level - ABIMN	pH Level - KIMN	pH Level - IMNIS
1	7.4	7.4	7.4
7	7.6	7.6	7.4
21	7.79	7.8	7.9
30	7.86	7.86	7.9

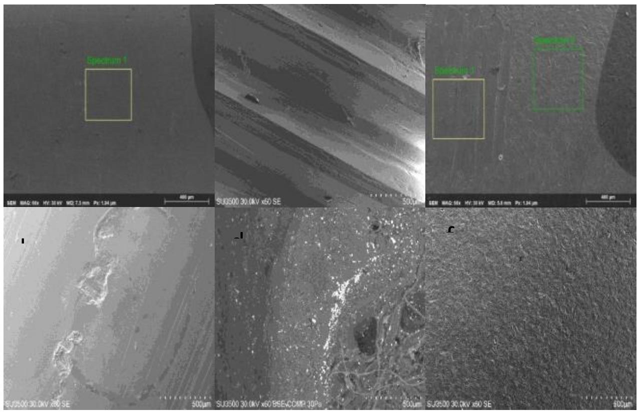


Figure 4: Scanning Electron Microscope Characterization of a-b) KIMN before and after 30 day immersion; c-d) ABIMN before and after 30 day immersion; e-f) IMNIS before and after 30 day immersion

Figure 4 shows the surface morphology of the nails used before and after the 30th day of immersion testing.

4. DISCUSSION

The ABIMN was designed to as a bridge to definitive intramedullary nailing after spanning external fixation of the tibia or femur in polytrauma patients with high injury severity score, as a part of damage control orthopaedics; damage control and salvage of a mangled limb to provide stabilization; prevent medullary osteomyelitis; and treatment of medullary osteomyelitis with infected prior nail [24]. Patients with treated with the ABIMN are usually instructed to do non-weight bearing or touch-down weight bearing w/ assistive devices and do active range of motion of adjacent joints, probably because the biomechanical properties of the ABIMN have never been defined.

The results indicate that median four point bending load (load needed to procedure a visible break or deformity of the IMN), median deflection at bending load and median Young's modulus of elasticity is significantly different across the three groups.

The median four point bending load, median deflection at bending load and median Young's modulus of elasticity were significantly lower in ABIMN regardless of its diameter, compared to KIMN (p=0.0027, p=0.0008, p=0.0027) and IMNIS (p=0.0025, p=0.0204, p=0.0025). The ABIMN being considered as a solid reamed IMN is significantly weaker in resisting bending forces, displaces easily under a given load and less stiff compared to KIMN and IMNIS. The median four point bending load of a ABIMN is 9.92% and 29.12% of that of the KIMN and IMNIS. The medial deflection at bending load of ABIMN is 46.73% and 47.72% of that of KIMN and IMNIS. Finally the Young's modulus of elasticity or the stiffness of AMBIN is only 11.37% and 18.90% of that of IMNIS.

There is also a very high positive correlation between bending rigidity and radius to the 4th power in ABIMN (r=0.9941, p value<0.00001). This is conforms with the observation that solid nails bending rigidity is proportional to its radius to the 4th power [25]. Use of a larger ABIMN is always recommended, but always take in mind that the ABIMN must always be removed after 6 weeks and replaced by a larger IMNIS for the definitive treatment. Make sure of the largest diameter IMNIS available per implant company.

4.1 Biomechanical Properties

4.1.1 Four Point Bending Load

There is no significant difference in the median four point bending load, median deflection at bending load and median Young's modulus of elasticity between KIMN and IMNIS (p=0.2166, p=0.4342, p=0.2166). In this study there is no sufficient evidence to conclude that KIMN and IMNIS have comparable load values. KIMN being considered as a hollow slotted IMN and IMNIS being considered as a hollow non slotted IMN have comparable three point and four point bending tests from the findings of Russell et. al., Beals et al. and Miles et al [26].

Median four point bending load significantly differ across groups (Table 3). These results indicate that the diameter of the antibiotic bone cement coating has an effect on the load that the ABIMN can withstand, rather that the stainless steel core diameter alone since this was held constant throughout all the samples of ABIMN at 4mm.

The median four point bending load of an ABIMN, regardless of the diameter is significantly lower than the IMNIS 10. All of the ABIMN except ABIMN 13 has a significantly lower median four point bending load compared to KIMN 11 and IMNIS 10. ABIMN 13 median four point bending load was only significantly lower than the IMNIS 10. The median four point bending load of ABMIN 10, ABIMN 11, ABIMN 12 and ABIMN 13 are 9.99% (439.36 N or 44.80 kgf), 8.61% (378.78 N or 38.62 kgf), 10.33% (454.19 N or 46.31 kgf) and 11.04% (485.62 N or 49.52 kgf) of that of the IMNIS 10 (4398.26 N or 448.50 kgf).

No significant difference between KIMN 10 and 11 (p=0.3040).

No significant difference between IMNIS and KIMN 10 (p=0.1779) and 11 (p=0.3540). This is also congruent with findings of Russell et. al., Beals et. al. and Miles et. al that three point and four point bending tests of hollow slotted nails and hollow slotted nails have comparable stiffness [26].

4.1.2 Deflection at Bending Load

The researchers were also able to measure the deflection at bending load, defined as the degree of which a structural element is displaced under load.

The median deflection at bending load of an ABIMN 11, ABIMN 12 and ABIMN 13 is significantly lower than KIMN 11. The median deflection at bending load of an ABIMN 12 and ABMIN 13 diameter is significantly lower than the KIMN 10, KIMN 11 and IMNIS 10. The median deflection at bending load of ABIMN 12 and ABIMN are 53.94% and 63.34% smaller than that of IMNIS 10.

No significant difference between KIMN 10 and 11 (p=0.2576).

No significant difference between IMNIS and KIMN 10 (p=0.4568) and 11 (p=0.3103).

4.1.3 Four Point Maximum Bending Load

Median Four Point Maximum Bending Load was only performed for ABIMN and was significantly different across the four groups. Only the ABIMN underwent the Four Point Maximum Bending Load testing, since the ABIMN is composed of two different materials to further establish that the diameter of the antibiotic bone cement coating has an effect on the load that the ABIMN can withstand, rather that the stainless steel core diameter alone since this was held constant throughout all the samples of ABIMN at 4mm. Further analysis showed that the median value of ABIMN 10 and ABIMN 11 were significantly lower compared to ABIMN 13 (p=0.0069, p=0.0066), not with other types (all p's>0.05). The median four point maximum load of ABIMN 10, ABIMN 11 and ABIMN 12 are only 70.42%, 68.88% and 89.90% compared to that of ABIMN 13.

No significant difference between ABIMN 12 and 13 (p=0.1340). A 12mm ABMIN and 13mm ABIMN have a comparable four point maximum bending load.

4.1.4 Young's Modulus of Elasticity

The stiffness of ABIMN 10 and ABIMN 11 were significantly lower than KIMN 10, KIMN 11 and IMINIS 10. ABIMIN 12 stiffness is significantly lower than KIMN 11 and IMNIS 10. ABIMN 10, ABIMN 11 and ABIMN 12 have only 8.67%, 9.59% and 11.38% of the stiffness of IMNIS 10.

No significant difference between IMNIS and KIMN 11 (p=0.3540)

4.1.5 Cyclic Axial Loading

Despite having no significant difference in median axial cyclic loading, breaking load the ABIMN 10, ABIMN 11 and ABIMN 12 can withstand 66.76% (943.33 N or 96.19 kgf), 64.75% (915 N or 93.30 kgf) and 88.18% (1246 N or 127.06 kgf) of that of the IMNIS 10 (1413 N or 144.09 kgf). This means that the ABIMN 10 , ABIMN 11 and ABIMN 12 can only withstand 42.75%, 41.47% and 56.47% of the body weight of a 75 kg man during walking for 6 weeks [27]. Weight bearing can safely be initiated from touch down weight bearing up to partial weight bearing up 25% of an average 75 kg man.

4.2 Surface Activity in SBF

Chemical testing revealed that the rod used for the ABIMN is stainless steel 304, KIMN is stainless steel 316 and IMNIS is titanium 6-4.

Corrosion or Immersion testing of the IMNs revealed an increase in the pH resulted from the build up of -OH ions brought by the exchange of positive ions in the IMNs samples and H+ ions from the SBF solution. This alkalinity also led to the formation of apatite whereon Ca^{+2} was bonded with the metal hydroxide and then later on with the PO_4^{-3} [28-30]. After this precipitate formation, pH level becomes more stable and then starts to decrease due to the consumption of -OH ions for the precipitate does not anymore contribute to the pH, thus making all the IMNs safe for human use.

The deposition of the apatite on the surface of all the IMN samples did not take place due to several factors like geometry, texture of the sample, surface treatment and SBF concentration [31].

The presence of pitting corrosion and red rust were observed on a small area of the KIMN after the 30th day of immersion testing which was common on stainless steel implants [32,33]. It was not observed on the ABIMN even if it is grade 304, may be due to the presence of antibiotic bone cement coating that covers the metallic parts of the sample and even the exposed parts exhibited better corrosion resistance. The coating of the IMNIS after the immersion testing was observed to have discoloration, but the titanium base exhibited no notable defects.

This means that the ABIMN is safe to use in terms of its chemical components. The ABMIN is also qualitatively comparable to KIMN during the corrosion testing producing almost the same pH levels during the observed period of time.

5. CONCLUSION

The median four point bending load, median deflection at bending load and median Young's modulus of elasticity were significantly lower in ABIMN regardless of its diameter compared to KIMN and IMNIS.

There is also a very high positive correlation between bending rigidity and radius to the 4th power in ABIMN. Bending rigidity of an ABIMN is proportional to its radius to the 4th power.

The median four point bending load of ABMIN 10, ABIMN 11, ABIMN 12 and ABIMN 13 are 9.99% (439.36 N or 44.80 kgf), 8.61% (378.78 N or 38.62 kgf), 10.33% (454.19 N or 46.31 kgf) and 11.04% (485.62 N or 49.52 kgf) of that of the IMNIS 10 (4398.26 N or 448.50 kgf).

The median deflection at bending load of ABIMN 12 and ABIMN are 53.94% and 63.34% smaller than that of IMNIS 10.

The median four point maximum load of ABIMN 10, ABIMN 11 and ABIMN 12 are only 70.42%, 68.88% and 89.90% compared to that of ABIMN 13. ABIMN 10, ABIMN 11 and ABIMN 12 have only 8.67%, 9.59% and 11.38% of the stiffness of IMNIS 10.

ABIMN 10, ABIMN 11 and ABIMN 12 can only withstand 42.75%, 41.47% and 56.47% of the body weight of a 75 kg man during walking for 6 weeks. [39] Weight bearing can safely be initiated from touch down weight bearing up to partial weight bearing up 25% of an average 75 kg man.

Chemical testing revealed that the rod used in ABIMN was classified as stainless steel 304. The ABMIN is also qualitatively comparable to KIMN during the corrosion testing producing almost the same pH levels during the observed period of time.

The biomechanical properties of the ABIMN are statically inferior to the KIMN and IMNS, but are now somehow defined. The chemical properties of the ABIMN revealed that it is safe to use and has qualitatively comparable corrosion properties to KIMN. The ABIMN can be left for 6 weeks, with the patient on partial weight bearing up to 25% of an average 75kg man. For easier removal of the ABIMN and after completion of both oral and IV antibiotics at 6 weeks post op; it still advisable to remove the ABIMN and perform exchange nailing at the said timeframe.

6. LIMITATIONS

This is a contract research study and due to the limited funds some of the findings of the study has shown no significant difference, especially in the cyclic axial loading, this is due to the small sample size of IMNs. The values of the four point bending and cyclic axial loading may seem small compared to the forces acting on the limb during normal walking, but the study only dealt with the IMN. Once the IMN are inserted into the intramedullary canal, this would create a new bone and IMN construct that could withstand greater forces compared the IMN alone.

7. RECOMMENDATIONS

This research can be used as guide to future studies that would test the biomechanical properties of an implant using the same test setup. It would be better if funding would be granted from a foundation, so that a biomechanical bone model and ABIMN construct can be tested ultimately leading to higher values.

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