Journal of Hard Tissue Biology 23[3] (2014) 317-322

CODEN-JHTBFF, ISSN 1341-7649

Original

The Biocompatibility of Nitinol in Knee Joint Spaces and Femoral Tunnels: An Experimental Study in Rats

Aydiner Kalaci[1), Vedat Uruc[1), Raif Özden[1), Ibrahim Gökhan Duman[1), Yunus Dogramaci[1), Serhat Karapinar[1) and Mehmet Yaldiz[2)

[1) *Department of Orthopedics and Traumatology, Mustafa Kemal University Faculty of Medicine, Antakya, Turkey*
[2) *Department of Pathology; Mustafa Kemal University Faculty of Medicine, Antakya, Turkey*
(Accepted for publication, April 29, 2014)

Abstract: Currently the most common method of reconstructing a ruptured anterior cruciate ligament (ACL) is by using bone-patellar tendon-bone (BPTB) or semitendinosus, gracilis tendon autografts. Although good results are reported, donor morbidity continues to be a problem. To overcome these complications, synthetic grafts have been investigated. However, to date no prosthetic graft has been developed as an alternative to patellar or hamstring tendon autografts. The aim of the present study was to assess the biocompatibility of nitinol in rat knee joint spaces and distal femoral bones. Ten male, healthy Wistar albino rats, weighing between 300-350 g, were used. The right knee joint of each rat was reached by medial longitudinal parapatellar dissection. The femur distal was penetrated by a size 0.5 mm of Kirshner wires. Twenty nitinol wires were placed in the bone tunnel (0.125 mm in diameter and 5 mm long). In addition one nitinol wire was placed in the joint space. Following hemostasis, the layers were closed with interrupted sutures. The same procedure was repeated for the left side without placing any nitinol wire. The rats were allowed unrestricted weight bearing. Two animals died of unknown reasons during follow-up. The remaining rats were sacrificed 8 weeks after surgery. The knees were removed by careful dissection and the nitinol wires were removed. The sections taken from these specimens were stained with standard hematoxylin and eosin and with Mason trichrome and examined under the light microscope. The bone tunnels were filled with osteocytes and chondrocytes. In two specimens of the nitinol group, moderate synovitis was detected. The synovitis rate in the study group was found to be statistically insignificant. In conclusion, the short term biocompatibility of nitinol in the rat knee joint space and femoral tunnel was found to be within acceptable limits.

Key words: Anterior cruciate ligament; Biomaterials; Nitinol; Prosthetics; Synthetic grafts

Introduction

Anterior cruciate ligament (ACL) injuries are most commonly seen among young healthy individuals. Due to the surrounding synovial fluid and poor vessel supply ACL injuries cannot be treated neither conservatively nor by primer suturing[1)]. The current concept is to reconstruct the ruptured ACL most commonly by using Bone-patellar tendon-bone (BPTB) or hamstring autografts. Although good results are reported , some morbidities of donor sides including anterior knee pain, patellar tendonitis, infrapatellar contracture related with BPTB harvest and hamstring weakness, saphenous nerve injury related with hamstring harvest are reported[2,3)]. To overcome these complications, allografts and prosthetic grafts have been investigated. However, the use of allografts is not advantageous due to a limited donor tissue supply, delayed biological incorporation, risks of disease transmission and tissue rejection. Also, no synthetic graft could have been developed as an alternative to the patellar or hamstring tendon autografts.

Nitinol is a shape memory material which is constructed from nickel (Ni) and titanium (Ti). It was firstly developed at the Naval Ordinance Laboratories (NOL).The name originated with the merger of the abbreviations[4)]. Nitinol (NiTi) has shape memory, superelasticity and high damping properties [4)]. It has been used in cardiovascular surgery, otolaryngology, ophthalmology and general surgery[5-7)]. In orthopaedic surgery; plates, intramedullary nails staples, special designed expanding implants, porous implants as bone graft substitute, cervical disc prosthesis, vertebral rods made out of nitinol are are currently used[8-16)]. To date, it has not been used intraarticularly. We hypothesized that nitinol may be used in ACL reconstruction. The aim of this study was to investigate the biocompatibility of nitinol in rat knee joint space and distal femoral bone.

Correspondence to: Dr. Vedat Uruc, Department of Orthopedics and Traumatology, Mustafa Kemal University Faculty of Medicine, Antakya, Hatay, Turkey; Phone: +90 553 321 20 45; E-mail: urucvedat@gmail.com

Materials and Methods

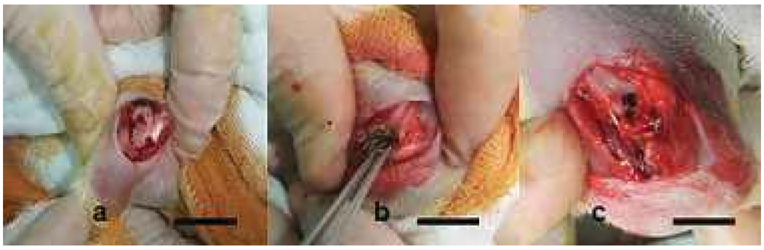

Figure 1: (a) medial parapatellar incision for knee arthrotomy, scale bar: 20 mm; (b) placing nitinol wires in the femoral tunnel, scale bar: 15 mm; (c) the appearance after placing the wires, scale bar: 10 mm

Figure 2: The nitinol wires 0.125 mm in diameter and 5 mm long, scale bar: 10 mm

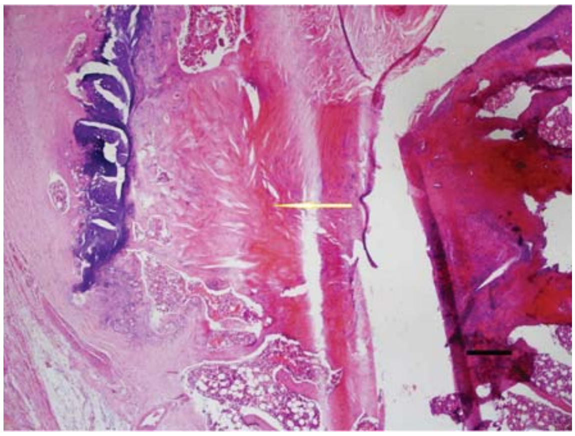

Figure 3. Hematoxylene-eosine × 200 stain of study group, scale bar: 30 µm. The femoral tunnel is filled by osteocytes and chonrocytes.

Figure 4: Hematoxylene-eosine ~200 stain of study group, scale bar: 30µm. Mild to moderate synovitis is seen.

Ten male, healthy wistar albino rats, weighing between 300-350 g were used. The study protocol was performed in accordance with the Guide for the Care and Use of Laboratory Animals, and was reviewed and accepted by the institutional animal care and usage committee. The both limbs were shaved and cleaned by Betadine (povidone-iodine) solution. The right knee of each rat was exposed via an anterior skin incision under ketamine hydrochloride anesthesia. Following the skin incision the knee joint was reached by medial longitudinal parapatellar dissection (Fig. 1a). The femur distal was penetrated by a size 0.5 mm of Kirshner wire. Fifty nitinol wires, 0.125 mm in diameter and 5mm long (Fig. 2), were placed in the bone tunnel (Fig. 1b, c). In addition one wire was placed in the joint space. Following hemostasis, the layers were closed with interrupted sutures. The same procedure was repeated for the left side without placing any Nitinol wire.

The rats were allowed unrestricted weight bearing after recovery from the anesthesia. These animals were kept in individual cages and allowed free access to tap water and a standard pellet diet. The cages were housed in a temperature of 24 ^{o}C, humid air (55 %) and 12 hours of day/night light controlled room. Two animals died of unknown reasons during follow-up. No surgical wound infection was detected. The remaining rats were sacrificed 8 weeks after surgery. The knees were removed by careful dissection. Sixteen knees (8 from control group, 8 from Nitinol group) were prepared for histological examination. The specimens were fixed in 10 % neutral buffered formaldehyde for 2 days. The specimens were decalcified with 1.5 % aqueous hydrochloric acid for 3 days. After the Nitinol wires were removed the specimens were embedded in paraffin that allows obtaining 5-micron sections from each block and stained with hematoxylene eosin and Mason trichrome. The specimens were cut sagitally. Both groups were evaluated blindly by two senior pathologists under light microscopy

Statistical analysis

Statistical Package for Social Sciences (SPSS) for Windows version 18.0 was used for statistical analysis. Two groups were compared by Fisher's exact test. $p<0.05$ was considered as significant for all statistical data.

Results

Nitinol wires could be removed with difficulty. The bone tunnels were filled with reactive osteocytes and chondrocytes (Fig. 3). In two specimens of the Nitinol group moderate to severe synovitis were detected (Fig. 4). Two groups were statistically similar in terms of the rate of synovitis ($p=0.467$)

Discussion

In this study we found that the short-term biocompatibility of Nitinol both in distal femoral tunnel and in the joint space were in acceptable limits.

Although the investigations on ACL prosthesis has been continuing for a long time, no material could have been developed as an alternative for either hamstring or BPTB grafts. Up to date, some of the reported ACL prosthesis are; carbon fiber prosthetics, gore-tex permanent prosthesis, dacron, leeds-keio artificial ligament, kennedy ligament augmentation device (LAD), ligament advanced reinforcement system (LARS) artificial ligament, tissue-engineered scaffolds[17]. In the use of Carbon fiber prosthetics, migration of carbon wear particles into the joint space and regional lymph nodes are reported[18]. To overcome this problem Alexander et al. Coated the carbon fiber prosthetics with a co-polymer of polylactic acid (PLA) and polycapralactone[19]. However the long term results are unacceptable due to the high rate of rupture and poor functional outcomes[20,21]. It is reported that the ACL reconstructions with Gore-Tex were three times more strength than normal ACL, but unacceptable loosening were reported in the long term follow up[22-25]. Inspired by the use of Dacron grafts with success as a vascular surgery implant, various forms of Dacron grafts have been developed as a scaffold for ACL replacements. Although the short term results were satisfactory the long term functional results were poor. Likewise high rates of ligament ruptures in the long time follow up were reported with Leeds-Keio Artificial Ligament[26]. Kennedy Ligament Augmentation Device was developed for the protection of the autograft from excessive stresses during the initial phase in order to obtain earlier resumption of pre-operative activity levels[27]. However its use was abandoned due to intraarticular inflammation and synovitis[28]. The Ligament Advanced Reinforcement System (LARS) consists of fibers made of polyethylene terephthalate (PET). Residue laxity is reported after ACL reconstruction with this material[29-35]. Ventura et al reported 19 year follow up results of ACL reconstruction with PET and concluded that high rates of osteoarthritis and total ruptures were seen[36]. Some in vitro studies investigating fibroblast-seeded synthetic scaffolds and collagen-based prosthetics are also conducted on[37,38].

In the light of the data given above we can say that the main two problems of synthetic ACL grafts are functional insufficiency in long term and intraarticular inflammatory response.

Nitinol (NiTi) is a bio-implant material which key features are shape memory effect, super elasticity and high shock absorbing properties. Also it has the most closest elastic modulus to that of bone[16,39-42].

Singh et all reported the long term results of 133 NiTi clips used in 119 patients after cervical discoidectomy and concluded that these clips are accepted well by human tissue and do not interfere with MRI[43]. Kapanen et al investigated the biocompatibility of nitinol in osteoblast-like ROS-17 cell cultures and reported good results[44]. They also reported an animal study in which the effect of nitinol, stainless steel and titanium aluminium (6 %) vanadium (4 %) alloy (Ti-6Al-4V) on bone formation were compared and concluded that between implant groups the new bone area was largest in NiTi and had good biocompatibility[45]. In an animal study porous Nitinol alloy with porosity of 66.1 % showed 51 % bone contact[42]. Our study is the first one which investigates the intraarticular biocompatibility of Nitinol. The filling of the femoral tunnel with bone tissue, the difficulty of removing the wires, supported good bone biocompatibility and bone in-growth properties of Nitinol. This is also important for the stability of ACL reconstruction. We also think that the elasticity of Nitinol may be an advantage for good long term functional outcomes. Further biomechanical and clinical studies are needed to prove it.

The limitations of our study are the relatively small sample size due to ethical problems and the lack of biomechanical testings.

In conclusion the short term biocompatibility of Nitinol in the rat knee joint space and femoral tunnel was found to be in acceptable limits.

References

1. Nau T, Lavoie P and Duval N. A new generation of artificial ligaments in reconstruction of the anterior cruciate ligament. Two-year follow-up of a randomised trial. J Bone Joint Surg Br 84: 356-360, 2002
2. Rathbone S, Maffulli N and Cartmell SH. Most british surgeons would consider using a tissue-engineered anterior cruciate ligament: a questionnaire study. Stem Cells Int 2012; 2012:303724. doi: 10.1155/2012/303724.
3. Kartus J, Movin T and Karlsson J. Donor-site morbidity and anterior knee problems after anterior cruciate ligament reconstruction using autografts. Arthroscopy 17: 971-980, 2001
4. Mayo I and Kauffman G. The Story of Nitinol: The serendipitous discovery of the memory metal and its applications. Springer-Verlag Inc., New York, 1996
5. Berrevoet F, Vanlander A, Bontinck J and Troisi RI. Open preperitoneal mesh repair of inguinal hernias using a mesh

with nitinol memory frame. Hernia 17: 365-371, 2013
6. Karabulut M, Bas K, Gonenc M, Uygar Kalayci M, Abdussamet Bozkurt M, Baha Temizgonul K and Alis H. Self-expanding metallic stents in acute mechanical intestinal obstructions resulting from colorectal malignancies. Am Surg 79: 1279-1282, 2013
7. Roosli C and Huber AM. Mid-term results after a newly designed nitinol stapes prosthesis use in 46 patients. Otol Neurotol 34: 61-64, 2013
8. Kok D, Donk RD, Wapstra FH and Veldhuizen AG. The memory metal minimal access cage: a new concept in lumbar interbody fusion-a prospective, noncomparative study to evaluate the safety and performance. 2012;2012:898606. doi: 10.1155/2012/898606.
9. Kamysz JW. Percutaneous repair of a nonunion pubic ramus fracture using a metallic stent scaffold and cement osteoplasty. J Vasc Interv Radiol 21: 1313-1316, 2010
10. Olender G, Pfeifer R, Muller CW, Gosling T, Barcikowski S and Hurschler C. A preliminary study of bending stiffness alteration in shape changing nitinol plates for fracture fixation. Ann Biomed Eng 39: 1546-1554, 2011
11. Tarnita D, Tarnita DN, Bizdoaca N, Tarnita C, Berceanu C and Boborelu C. Modular adaptive bone plate for humerus bone osteosynthesis. Rom J Morphol Embryol 50: 447-452, 2009
12. Tarnita D, Tarnita DN, Hacman L, Copilus C and Berceanu C. In vitro experiment of the modular orthopedic plate based on Nitinol, used for human radius bone fractures. Rom J Morphol Embryol 51: 315-320, 2010
13. Tarnita D, Tarnita DN, Popa D, Grecu D, Tarnita R, Niculescu D and Cismaru F. Numerical simulations of human tibia osteosynthesis using modular plates based on Nitinol staples. Rom J Morphol Embryol 51: 145-150, 2010
14. van Kampen RJ, Thoreson AR, Knutson NJ, Hale JE and Moran SL. Comparison of a new intramedullary scaffold to volar plating for treatment of distal radius fractures. J Orthop Trauma 27: 535-541, 2013.
15. Winkel R and Schlageter M. Nitinol shape memory staple for osteosynthesis of the scaphoid. Oper Orthop Traumatol 21: 361-372, 2009
16. Xin-wei L, Shuo-gui X, Chun-cai Z, Qing-ge F and Pan-feng W. Biomechanical study of posterior wall acetabular fracture fixation using acetabular tridimensional memory alloy-fixation system. Clin Biomech 25: 312-317, 2010
17. Mascarenhas R and MacDonald PB. Anterior cruciate ligament reconstruction: A look at prosthetics—past, present and possible future. Mcgill J Med 11: 29-37, 2008
18. Jenkins DH. The repair of cruciate ligaments with flexible carbon fibre. A longer term study of the induction of new ligaments and of the fate of the implanted carbon. J Bone Joint Surg Br 60: 520-522, 1978
19. Alexander H, Weiss AB and Parsons JR. Absorbable polymer-filamentous carbon composites—a new class of tissue scaffolding materials. Aktuelle Probl Chir Orthop 26: 78-91, 1983
20. Campbell AC and Rae PS. Anterior cruciate reconstruction with the ABC carbon and polyester prosthetic ligament. Ann R Coll Surg Engl 77: 349-350, 1995
21. Mody BS, Howard L, Harding ML, Parmar HV and Learmonth DJ. The ABC carbon and polyester prosthetic ligament for ACL-deficient knees. Early results in 31 cases. J Bone Joint Surg Br 75: 818-821, 1993
22. Bolton CW and Bruchman WC. The GORE-TEX expanded polytetrafluoroethylene prosthetic ligament. An in vitro and in vivo evaluation. Clin Orthop Relat Res 196: 202-213, 1985
23. Glousman R, Shields C, Jr., Kerlan R, Jobe F, Lombardo S, Yocum L, Tibone J and Gambardella R. Gore-Tex prosthetic ligament in anterior cruciate deficient knees. Am J Sports Med 16: 321-326, 1988
24. Indelicato PA, Pascale MS and Huegel MO. Early experience with the GORE-TEX polytetrafluoroethylene anterior cruciate ligament prosthesis. Am J Sports Med 17: 55-52, 1989
25. Woods GA, Indelicato PA and Prevot TJ. The Gore-Tex anterior cruciate ligament prosthesis. Two versus three year results. Am J Sports Med 19: 48-55, 1991
26. Murray AW and Macnicol MF. 10-16 year results of Leeds-Keio anterior cruciate ligament reconstruction. Knee 11: 9-14, 2004
27. Kennedy JC, Roth JH, Mendenhall HV and Sanford JB. Presidential address. Intraarticular replacement in the anterior cruciate ligament-deficient knee. Am J Sports Med 8: 1-8, 1980
28. Kumar K and Maffulli N. The ligament augmentation device: an historical perspective. Arthroscopy 15: 422-432, 1999.
29. Huang JM, Liu HY, Chen FR, Jian GJ, Chen Q, Wang ZM and Kang YF. Characteristics of bone tunnel changes after anterior cruciate ligament reconstruction using Ligament Advanced Reinforcement System artificial ligament. Chin Med J 125: 3961-3965, 2012
30. Ji T, Tang X and Guo W. The use of Ligament Advanced Reinforcement System (LARS) in limb salvage surgery: A pilot clinical study. J Arthroplasty 28: 892-894, 2013
31. Pan X, Wen H, Wang L and Ge T. Bone-patellar tendon-bone autograft versus LARS artificial ligament for anterior cruciate ligament reconstruction. Eur J Orthop Surg Traumatol 23: 819-823, 2013
32. Smith C, Ajuied A, Wong F, Norris M, Back D and Davies A. The use of the ligament augmentation and reconstruction

system (LARS) for posterior cruciate reconstruction. Arthroscopy 30: 111-120, 2014

33. Tao J, Li X, Zhou Z and Zhu Z. Acute single-stage reconstruction of multiligament knee injuries using the ligament advanced reinforcement system. Med Princ Pract 22: 373-378, 2013
34. Vaquette C, Viateau V, Guerard S, Anagnostou F, Manassero M, Castner DG and Migonney V. The effect of polystyrene sodium sulfonate grafting on polyethylene terephthalate artificial ligaments on in vitro mineralisation and in vivo bone tissue integration. Biomaterials 34: 7048-7063, 2013
35. Viateau V, Manassero M, Anagnostou F, Guerard S, Mitton D, andMigonney V. Biological and biomechanical evaluation of the ligament advanced reinforcement system (LARS AC) in a sheep model of anterior cruciate ligament replacement: a 3-month and 12-month study. Arthroscopy 29: 1079-1088, 2013
36. Ventura A, Terzaghi C, Legnani C, Borgo E and Albisetti W. Synthetic grafts for anterior cruciate ligament rupture: 19-year outcome study. The Knee 17: 108-113, 2010
37. Bourke SL, Kohn J and Dunn MG. Preliminary development of a novel resorbable synthetic polymer fiber scaffold for anterior cruciate ligament reconstruction. Tissue Eng 10: 43-52, 2004
38. Caruso AB and Dunn MG. Changes in mechanical properties and cellularity during long-term culture of collagen fiber ACL reconstruction scaffolds. J Biomed Mater Res A 73: 388-397, 2005
39. Launey M, Robertson SW, Vien L, Senthilnathan K, Chintapalli P and Pelton AR. Influence of microstructural purity on the bending fatigue behavior of VAR-melted superelastic Nitinol. J Mech Behav Biomed Mater 10: 181-186, 2014
40. McKelvey AL and Ritchie RO. Fatigue-crack propagation in Nitinol, a shape-memory and superelastic endovascular stent material. J Biomed Mater Res 47: 301-308, 1999
41. Miura F, Mogi M, Ohura Y and Hamanaka H. The super-elastic property of the Japanese NiTi alloy wire for use in orthodontics. Am J Orthod Dentofacial Orthop 90: 1-10, 1986
42. Kujala S, Ryhanen J, Danilov A and Tuukkanen J. Effect of porosity on the osteointegration and bone ingrowth of a weight-bearing nickel-titanium bone graft substitute. Biomaterials 24: 4691-4697, 2003
43. Singh D, Sinha S, Singh H, Jagetia A, Gupta S, Gangoo P and Tandon M. Use of nitinol shape memory alloy staples (NiTi clips) after cervical discoidectomy: minimally invasive instrumentation and long-term results. Minim Invasive Neurosurg 54: 172-178, 2011
44. Kapanen A, Ilvesaro J, Danilov A, Ryhanen J, Lehenkari P and Tuukkanen J. Behaviour of nitinol in osteoblast-like ROS-17 cell cultures. Biomaterials 23: 645-650, 2002
45. Kapanen A, Ryhanen J, Danilov A and Tuukkanen J. Effect of nickel-titanium shape memory metal alloy on bone formation. Biomaterials 22: 2475-2480, 2001