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Joint Pressure, Volume and Alignment in Development of AOA: Indications for Orthobiologics and Surgeons

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Abstract

To fix and prevent, not 'manage' Osteoarthritis OA in the lower limb, should be the collective 'Holy Grail' with or without Orthobiologics OB. Lateral Ankle Sprain LAS, Chronic Ankle Instability CAI and Ankle Osteoarthritis AOA create asymmetry which alters the biomechanics of the entire lower limb, so by better addressing AOA, we can probably do more than just impact the multi-billion dollar annual costs of AOA.

It would seem we have advanced, if not futuristic Surgical techniques and Orthobiologic technology, so what is missing? The short answer is Medical Intent MI. Devices and methods used in rehabilitation need MI intent to enable and stimulate repair. The world is changing and Morals Ethics and the human costs, are being counted. CTE concussion is just the tip of the iceberg for cumulative trauma injuries, in cost and prevalence, and class actions seek to defend and enforce people's rights to safety, either in the workplace, as in professional sport, or in medical outcomes.

The significant yet hidden role of the subtalar joint as a 'Safety Valve' was first noted by Albert Ferguson in 1972, yet today the contradictions in rehabilitation and injury prevention devices that restrict the STJ, remain commonplace. It is also necessary to consider what has changed inside the synovial capsule before and after lateral ligament injury, such as pressure, joint alignment and space, so we can better understand and design for restoration of homeostasis.

This paper will examine factors, causes and interventions that may be inadvertently restricting or preventing Orthobiologics effectiveness in the human ankle from a Translational Medicine perspective and an engineering bias.

Keywords

Orthopaedic; Orthopedic Ankle Surgeon; Subtalar; Talocrural; Tibiotalar; CAI; LAS; Osteoarthritis

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Abbreviation

OB: Orthobiologic; **OA:** Ankle Osteoarthritis; **PTAOA:** Post-traumatic Ankle Osteoarthritis; **LAS:** Lateral Ankle Sprain; **CAI:** Chronic Ankle Instability; **MI:** Medical Intent; **CTE:** Chronic Traumatic Encephalopathy; **NFL:** National Football League; **STJ:** Subtalar Joint; **TJ:** Talocrural Joint (also known as Tibiotalar Joint); **ROM:** Range of motion; **OLT:** Osteochondral lesion of the Talus; **IABP:** Intra-articular barometric pressure; **TSJ:** Talocrural synovial joint; **SF:** Synovial fluid; **VP:** Vacuum Phenomenon; **DCS:** Decompression Sickness or The Bends; **HA_S:** High-molar-mass hyaluronans; **PPE:** Personal protective equipment; **RTP:** Return to play; **PLP:** Point Loading Pain; **LSP:** Ligament Stretch Pain; **AT:** Athletic trainers

Introduction

Far too often, the combination of the two separate joints, the talocrural joint TJ and the subtalar joint STJ, are miss-represented or ignored, most importantly in past and current rehabilitation protocols, orthosis design and associated marketing. The role and 'roll' of the STJ in inversion and extreme force transfer between two non-parallel planes of motion (lower leg Frontal plane-foot/ground Transverse plane) must be understood and respected. "Not surprisingly, we are seeing that patients with a history of LAS and CAI dominate ankle joint post-traumatic osteoarthritis (PTOA) cases, which comprise the majority of ankle joint OA surgical cases. Additionally, the onset of ankle joint PTOA is occurring earlier in one's lifespan than most would assume" [1]. The costs of treating ankle injuries in the USA is estimated to be in excess of $6.2 billion in annual costs [2].

Ankle function

"The ankle joint is a hinged synovial joint with primarily up-and-down movement (plantarflexion and dorsiflexion). However, when the range of motion of the ankle and subtalar joints (talocalcaneal and talocalcaneonavicular) is taken together, the complex functions as a universal joint" (Figure 1,2) [3].

Figure 1: The obliquity of the ankle and the subtalar axes. (a) Anterior view (b) Lateral view (c) Top view.

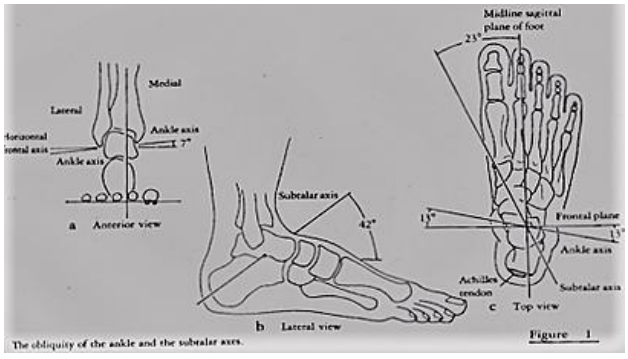

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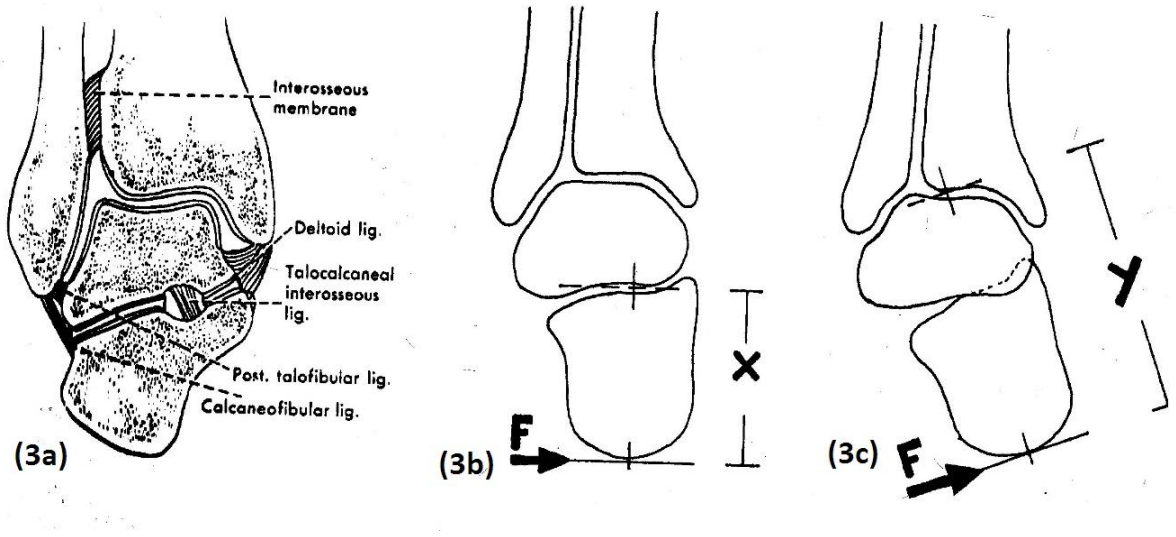
Figure 2: Socket set Universal joint and car drive train.

Lateral Ankle Sprain LAS Mechanism

"The AJ rather than the STJ is likely to be damaged during inversion stress since the thick and strong inter osseous talocalcaneal ligament (internal) and the joint capsule which maintain the joint's integrity are both close to the axis and to the applied force (Figure 3a). When an inverting force is applied to the calcaneus a rotary torque is created about the STJ axis (Figure 3b) along the moment arm X. When the limit of STJ motion is reached, the calcaneus and talus would then become a rigid lever Y (Figure 3c). The torque is then transmitted to the ankle joint [talocrural] along this longer moment arm Y" [4].

Figure 3: (3a) Frontal section through the talocrural and subtalar joints. **(3b)** Representation of a laterally applied force along moment arm X inverting the calcaneous. **(3c)** Same force transferred to the ankle joint at the limit of subtalar ROM along moment arm Y.



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"During a lateral ankle sprain the anterior talofibular ligament ruptures first as the limit of STJ ROM is reached, allowing the fibula to slide posteriorly, releasing the leg to externally rotate. As Rotation progresses, the calcaneofibular ligament is stressed and is the next to rupture. As this happens the loading appears to shift to the medial dorsal talus. This observation is consistent with the findings of Bruns and Rosenback (40) who demonstrated pressure increases on the medial talar border at a similar stage of ligament dissection. Along with other researchers, they have related the incidence of posteromedial osteochondral lesions to a history of lateral ankle sprains" [4].

Steele JR et al. recommend more "research is needed surrounding pathophysiology of osteochondral lesions of the talus. This may allow for the development of improved treatments and preventive treatment options to help decrease the incidence of OLTs. For example, injectable treatments that target the inflammatory cascade or promote natural chondrocyte repair or regeneration may be a future option to help prevent the development of OLTs after acute ankle injury. The current operative treatments were tabled into three groups, cartilage repair, cartilage regeneration and cartilage replacement strategies" [5].

Rehabilitation and Prevention methods based on'Prohibition'

Restricting the STJ range of motion ROM or inversion, is a current goal of many orthoses worn to 'support' and 'protect' injured ankles either through rehab and/or on return to play RTP. From an engineering perspective, the logical rotary compensation at the TJ to accommodate restriction of the STJ, actually compromises damaged lateral ligaments, and creates a 'mortar and pestle' effect within the ankle mortis, contributing to medial talar dome insult. This leads me to contend that systems based on STJ ROM restriction are not assisting the rehab process at all. In fact, their lack of Medical Intent MI (explored in Discussion) may be why what appear to be efficacious Orthobiologic and Surgical techniques, aren't able to stem the tide of AOA.

The talocrural joint TJ

The functioning TJ is co-dependent upon environmental factors and loads, such that small changes in either, would likely set off a sequela of adverse events, possibly culminating in AOA. If we understand more of what 'normal' *function* is from a Translational Medicine perspective, the *form* of interventions to prevent or reverse these changes, may become clearer.

Intra-articular barometric pressure IABP changes inside the synovial capsule, in healthy and post injury/surgery talocrural joints, interests me, not only how that may influence maintenance and repair functions, but most importantly, how do they influence engineering functions? Is the pneumatic function of the intact and 'inflated' talocrural synovial joint TSJ, like a tire on a car, essential to motion and shock absorbency?

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Intra-articular barometric pressure IABP in the Talocrural SJ

Firstly, I will focus on the effects of IABP changes, in the normal state, and later postulate as to what may be happening in the injured or diseased state. In the normal healthy TJ we can approximate how pressure changes from weight bearing WB (compression) to swing phase (traction through foot weight + rotary inertia) using the equation P=F/A. P is the barometric pressure we are measuring, F=m·a is the force (body weight BW (m) x (a) gravity G) and A is the tibio-fibular contact area of the talus. For simplicity of the example we will consider the static loaded and unloaded states of a single leg stance of a 100 kg subject in neutral position, ignoring inertia from linear and rotary motion, for now. We will also assume the walls of the capsule are not flexible but note that they are somewhat, indicating a further 'hydraulic' function with engineering intent.

Millington et al. used stereophotography to calculate the mean (n=10) talar contact area in the neutral position under a load of 1000N (102 kg) [6]. For the purpose of this example I will use the approximate value of 9 cm^2 (0.0009 m^2) the area over which the force is applied, and assume that the baseline resting TJ IABP in Pascals Pa is 0 $kg{\cdot}m^{-1}{\cdot}s^{-2}$ to approximate intra-articular barometric pressure using (Pressure) = F (force) / A (area) (Table 1).

Table 1: Intra-articular barometric pressure for 100 kg single leg stance P_{+ve} and non-weightbearing P_{-ve}

P = F/A where F = m·a and A, the area of talus = 0.0009 m^2	P_0 = 0 $kg{\cdot}m^{-1}{\cdot}s^{-2}$
Static single leg stance barometric pressure is; $P_{+ve} = m_{+ve}{\cdot}a/A$ = 100 × 9.81/0.0009 = 1090000 $kg{\cdot}m^{-1}{\cdot}s^{-2}$ P_{+ve} = 1090 kPa (1.09 MPa) or 158.1 psi	P_{+ve} = ? m_{+ve} mass (BW) = 100 kg P_{+ve} = ? a acceleration = 9.81 $m{\cdot}s^{-2}$ A area of talus = 0.0009 m^2 m_{+ve} BW = 100 kg
Static foot weight non-WB barometric pressure is; $P_{-ve} = m_{-ve}{\cdot}a/A$ = -1 × 9.81/0.0009 = -10900 $kg{\cdot}m^{-1}{\cdot}s^{-2}$ = -10.9 kPa or -1.6 psi	P_{-ve} = ? m_{-ve} mass (foot/shoe) = -1 kg a acceleration = 9.81 $m{\cdot}s^{-2}$ A area of talus = 0.0009 m^2

From this example, we can see that the pressure differences between single leg stance loaded and unloaded is 1.1 MPa (158 psi), which to put in perspective, is equivalent to being under over 120 meters of water [7], and then in a split second, surfacing. In a continuous cycle, this

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would be fine and likely advantageous (homeostasis), but if that pressure was released and not restored, the consequences could be widespread. Typically, 193-234 kPa (28-32 psi) is the amount of pressure you would inflate your car tire to, however, a truck tire, carrying bigger loads, has stronger construction and higher pressures [8].

We might expect the TJ IABP to increase with load (BW & activity), with obvious increased loaded peaks, but does increased load and activity lead to a higher resting pressure? Whilst it has been a challenge finding research regarding TJ IABP for this review, I did find some indications of similarities between AOA and Decompression Sickness, or The Bends, for example, the Vacuum Phenomenon VP, possibly worth considering.

"The VP is a combination of anatomy and physics, calling into play both Henry's Law and Boyle's Law through hydrodynamic cavitation [2,4]. Simply put, gas precipitates out of solution through a negative intra-articular pressure when a joint is distended (e.g. traction) or collapses. The newly created free space within the joint capsule needs to be filled, and is done so by gas (primarily nitrogen) [2,3]. In this situation it is often by a gaseous element that precipitates out of the local tissue or synovial fluid due to changes in pressure [1,2,4]. Gohil et al and Yanagawa et al provide detailed explanations of this phenomenon. Normally, this gas goes back into solution when the joint returns to its normal volume and pressure. However, in situations of arthritis, a thickened or fibrotic/scarred joint capsule does not allow the gas to dissolve out" [9]. This may imply that restoration of normal TJ alignment, volume, pressure, load and a healthy joint capsule, are necessary to restore hydrostatic and osmotic balance. "The bends, also known as decompression sickness (DCS) or Caisson disease, occurs in scuba divers or high altitude or aerospace events when dissolved gases (mainly nitrogen) come out of solution in bubbles and can affect just about any body area including joints, lung, heart, skin and brain. Decompression sickness (DCS) is caused by the formation of bubbles of gas that occur with changes in pressure during scuba diving" [10]. "Dysbaric osteonecrosis is a serious complication for those exposed to a hyperbaric environment, with prevalence of 17% amongst compressed air workers and 4.2% amongst divers. Bone lesions are characteristically multiple and bilateral, occurring frequently in the shafts of the femora or tibiae and the heads of the humeri or femora. A proportion of the lesions will lie next to the joint surface, the so-called juxta-articular lesion, and these may progress to a structural failure and secondary osteoarthritis" [11]. We need to look more closely at the function and composition of the synovial capsule and synovial fluid itself.

Hyaluronan and synovial joint function

Orthopaediczone.org discusses the lubrication properties of SF but also suggests a function in shock absorbency. "Synovial fluid exhibits non-Newtonian flow characteristics. The viscosity coefficient is not a constant, and the fluid is not linearly viscous. Instead, it exhibits thixotropic characteristics. The synovial fluid in diarthrotic joints becomes thick the moment

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shear is applied in order to protect the joint and subsequently thins to normal viscosity to resume its lubricating function between shocks" [12].

"A non-Newtonian fluid is a fluid whose viscosity is variable based on applied stress or force. The most common everyday example of a non-Newtonian fluid is cornstarch dissolved in water. Behavior of Newtonian fluids like water can be described exclusively by temperature and pressure. However, the physical behavior of non-Newtonian fluid depends on the forces acting on it from second to second. If you punch a bucket full of non-Newtonian fluid such as cornstarch, the stress introduced by the incoming force causes the atoms in the fluid to rearrange such that it behaves like a solid. Your hand will not go through. If you shove your hand into the fluid slowly, however, it will penetrate successfully" [13].

As synovial fluid SF is a non-Newtonian fluid, we can expect changed properties with variations in temperature, volume, pressure and the rate at which the force is applied (Inertia $I=F/(t_2–t_1)$). The takeaway here is that SF can change from liquid lubricant to semi-solid shock absorber and joint space retainer, depending on the conditions.

Tamar TM describes synovial joint function and the distribution, properties and applications of hyaluronan in SF [14]. The following are of relevance to our discussion today.

"The synovial fluid (SF) of natural joints normally functions as a biological lubricant as well as a biochemical pool through which nutrients and regulatory cytokines traverse. SF contains molecules that provide low-friction and low-wear properties to articulating cartilage surfaces. As a biochemical depot, SF is an ultra-filtrate of blood plasma that is concentrated by virtue of its filtration through the synovial membrane. Each synovial joint is surrounded by a fibrous, highly vascular capsule/envelope called synovium; whose internal surface layer is lined with a synovial membrane. Inside this membrane, type B synoviocytes (fibroblast-like cell lines) are localized/embedded. Their primary function is to continuously extrude high-molar-mass hyaluronans (HAs) into synovial fluid" [14]. The mechanisms responsible for continuous extrusion of HAs under extreme pressure differentials may well be compromised with loss of TJIABP, if not disabled entirely. Or worse, that same SF may be releasing harmful gases and 'agents', just like The Bends, when not under pressure.

Immobilization, Evolution and Rehabilitation contradictions

Put simply, immobilization is inconsistent with modern practice of early mobilization after repair in the knee, does not make 'evolutionary' sense because you would have died of starvation or become prey, and then there is rehabilitation. LAS rehab focuses on retraining time and STJ ROM dependent responses, and taping or restrictive bracing is avoided, because of their know effects on both. Then on return to play RTP, either or both are often employed, potentially negating the time and range dependent retraining?

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Primary and secondary prevention of AOA

There are two opportunities to affect the rate of PTAOA development, by primary LAS prevention and at the time of injury, and the following months. Prophylactic methods like tape and braces need properly and consistently applied safety standards like those that currently apply to other safety equipment like bicycle and football helmets, mouthguards and shin pads. This will hold the 'Injury Industry' to account, or at least inform consumers and Professional Sports employees, of the risks of cumulative trauma and potential life-long consequences. What is not considered is that when these systems are used on children and professional athletes/employees, they are actually Personal Protective Equipment PPE, and rather than be a choice, it is in fact, a legal responsibility.

Immediately upon occurrence of a LAS, we should be providing intra-articular support to minimize point loading pain PLP and ligament stretch pain LSP, the Biomechanics of Ankle Pain [15], and restore mobility and weight-bearing. If the synovial capsule has experienced traction, there may be potential for gases to come out of solution, which by weight bearing may dissolve back into solution. This must however be done without STJ restriction as this will lead to TJ rotary compensation, rather than optimal loading from restored safe motion.

Discussion

Medically, Kinematic intra-articular Support Systems KiSS^{TM} (or their prophylactic cousin Kinetic impulse Suppression Systems) can maintain the natural function, joint integrity and alignment of the TJ, but unless in the case of ligament and especially synovial capsule rupture, the joint is properly aligned, sealed and repressured, the best we can hope for is 'maintenance'. By more accurately considering even medial to lateral joint spacing in traction in conjunction with Anterior Draw to tension a Bronstrom repair for example, the noted and multi-functional mechanical advantages of SF are enabled for lubrication and shock absorbance. Because just like a car with poor wheel alignment, the tire will 'scrub out' on either the inside (medial) or the outside (lateral), unless treated, especially if the 'tire' is not inflated.

Surgeons might consider measures to reseal the lateral synovial capsule, from the inside and out considering the pressures noted above. Further, incorporated OBs, in their many existing forms, may become more effective in the 'hyperbaric' environment. Going forward, if it can be shown that intra-articular support can indeed create optimal loading of ligaments, then less invasive suturing of the damaged ligaments, assisted by OBs, might well become an option. Or in their new forms, OBs may provide options for sealing, repressuring and repairing the synovial capsules natural function, as well as improvements in ligament and cartilage repair. Doctors, Surgeons and those involved in the OBs industry, like the new generation of Kinematic intra-articular Support Systems KiSS^{TM}, all have medical intent MI; to help create an environment rich with stimuli based on a thorough understanding of disease, repair and

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regeneration. Collectively we are in the business of 'fixing', whilst others seem quite happy to 'maintain', as a successful business model. Ankle surgeons know more about ankle function and tissue repair than most health professionals, so could take a more active role in prescription of rehabilitation and MI devices, as they do with OBs, especially in the litigious environment that is Professional Sport.

Professional sporting organizations and government bodies should take more responsibility for the safety and wellbeing of their population's long term, through consistent regulation of safety and medical devices. For example, in Australia, a Class 1 medical device approval from the Federal Government by the Therapeutic Goods Association TGA, costs just over $500 AUD. Listing only requires self-registration and declaration, without evidence of therapeutic benefit or even manufacturing standards, meaning rigid strapping tape, in Australia, is a Class 1 medical device. Sports administrators, amateur and professional, need to understand LAS through PTAOA as the cumulative trauma injury that it is, and treat LAS with the same respect as concussion, or we are sure to see a repeat of the past NFL Chronic Traumatic Encephalopathy CTE lawsuits. Untreated ankles can lead to life-long issues with enormous yet seemingly hidden global health costs and harm. It is evident we have advanced surgical, Orthobiologic and now joint support technologies, so perhaps the 'next safe leap for mankind', via Translational Medicine and collaboration, is closer than we think.

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Author's Disclaimer

Craig J Hubbard is the inventor, manufacturer and distributor of KiSS^{TM} Ankle Systems under the brand KiSS Ankle Co. Biomechanics of Ankle Pain, Point Loading Pain PLP, Ligament Stretch Pain LSP, Medical Intent MI and KiSS^{TM} are inventions of the Author.

References

1. *Gribble PA, Bleakley CM, Caulfield BM, Docherty CL, Fourchet F, Fong DT, et al. Evidence review for the 2016 International Ankle Consortium consensus statement on the prevalence, impact and long-term consequences of lateral ankle sprains. Br J Sports Med. 2016;50(24):1496-1505.*
2. *Gribble PA, Bleakley CM, Caulfield BM, Docherty CL, Fourchet F, Fong DT, et al. 2016 consensus statement of the International Ankle Consortium: prevalence, impact and long-term consequences of lateral ankle sprains. Br J Sports Med. 2016;50(24):1493-1495.*
3. *Hoagland TM, Guest TR and Young CC. Ankle Joint Anatomy. Medscape. 2015,*

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4. *Hubbard CJ. Considerations for the design of the 'ideal' ankle orthosis. Unpublished thesis University of Wollongong. 1992.*
5. *Steele JR, Dekker TJ, Federer EA, Liles JL, Adams SB, Easley ME. Osteochondral Lesions of the Talus: Current Concepts in Diagnosis and Treatment. Foot and Ankle Orthopaedics. 2018;3(33):1-9.*
6. *Millington S, Grabner M, Wozelka R, Hurwitz S, Crandall J. A stereophotographic study of ankle joint contact area. J Orthop Res. 2007;25:1465-1473.*
7. *Convert MPa to meter of head- Conversion of Measurement Units.*
8. *The Physics Factbook. An encyclopedia of scientific essays: Kanonik A. Pressure In A Truck Tire.2003.*
9. *Hood CR Jr, Jackson WR, Floros RC Bernstein DA. The vacuum phenomenon in the ankle joint: Air bubbles on CT. J Foot Ankle. 2018;11(2):2.*
10. *Fell SD, Davis CP. Decompression Syndromes: The Bends.*
11. *Davidson JK. Dysbaric disorders: aseptic bone necrosis in tunnel workers and divers. Baillière's Clinical Rheumatology. 1989;3(1):1-23.*
12. *https://www.orthopaedicsone.com/display/Main/Synovial%20fluid*
13. *Non-Newtonian fluid. Copyright 2009 General Electric Company. Available: https://www.ge.com/press/scienceworkshop/docs/pdf/Non_Newtonian_Fluid_with_Standards.pdf*
14. *Tamar TM. Hyaluronan and synovial joint: function, distribution and healing. Interdisciplinary Toxicology. Interdiscip Toxicol. 2013;6(3):111-125.*
15. *Hubbard CJ. KiSS ankle paradigm 2018. Available: https://www.kissankle.co/kiss-ankle-paradim.*

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