

**A THERAPEUTIC ANALYSIS OF HYALURONAN FLUID FLOW IN
DAMAGED MEDIAL/LATERAL MENISCI IN ARTHRITIC PATIENTS**

A Thesis by

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I have examined the final copy of this Project for form and content and recommend that it be accepted in partial fulfillment of the requirement for the degree of Master of Science with a major in Mechanical Engineering.

Dr. T. S. Ravigururajan, Committee Chair

We have read this Project
and recommend its acceptance:

Dr. Brian Driessen, Committee Member

Dr. Michael Jorgensen, Committee Member

DEDICATION

To my mother

ACKNOWLEDGMENTS

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ABSTRACT

Osteoarthritis is a common type of arthritis that breaks down the joint tissue, known as cartilage. This causes the bones to rub against each other, causing pain and loss of movement especially in weight-bearing joints in the knees, hips, feet and the back. In recent years, synovial fluid therapy is often used in patients with Osteoarthritis, where the fluid is directly injected into the tissue which acts as a lubricant in the joint. The fluid is based on Hyaluronan (HA), a pure solution of sodium hyaluronate and is a natural constituent of the human body. This study deals with the simulation and analysis of the Fluid Therapy and an aim to optimize the procedure as a function of characteristics and also disease stage. The tissue or cartilage has been modeled as biphasic and the simulation has been done using Fluid-Structure interaction using Sysnoise, commercially available FEM software. Different case studies related to cartilage damage have been analyzed and the results have been compared with the actual therapeutic procedure of fluid therapy. The results are provided in terms of the fluid velocity that helps the fluid to void the space inside the cartilage or the synovial joint. During actual fluid therapy, the fluid is expected to void between a period of 7 – 14 days, which is why the injections are given either weekly or biweekly. Results show that few patients, suffering from arthritis, can experience relief for a period of up to six months with the help of fluid therapy, with appropriate quantity of fluid and the concentration of HA in the fluid among other conditions. The present work provides an opportunity to optimize the fluid therapy procedure based on parameters, such as fluid volume and its thermophysical properties. Results from the study indicate that treatment can be custom designed by considering the concentration of HA in the synovial fluid injection, its viscosity, the weight and condition

of the patient and the stage of the disease. With fluid therapy being considered increasingly, optimization procedure would be of valuable medical help and of substantial economic benefit to patients.

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NOMENCLATURE

A	cross-sectional
\mathbf{a}	radius of indenter
a	area of opening in cartilage
c_0	speed of sound
E	Young's modulus
E_S	Young's modulus
F_A	vector of nodal forces
F_i	external forces acting on the fluid
h	permeation distance
H_A	aggregate modulus
k	permeability
P	applied load
\mathbf{p}'	pressure fluctuation
ΔP	applied pressure difference
Q	volumetric flow rate
T_{ij}	Lighthill stress tensor containing momentum flux, thermal and viscous terms
\bar{u}	particle density in x-direction
v	velocity of fluid oozing out of the cartilage
ν_S	Poisson's ratio
w_0	depth of penetration
	instantaneous density
\mathcal{V}	volume of fluid

CHAPTER 1

INTRODUCTION

Articular cartilage forms the bearing surfaces in synovial joints. Synovial joints are freely moving joints containing synovial fluid within the cartilage. Examples of such joints are the hip, knee shoulder, etc. In humans, the articular cartilage is normally between 1 and 5mm thick, depending on the individuals. It consists of a liquid phase, which is in the form of interstitial water, within a solid phase or a synovial tissue (Goldsmith, 1996). Figure 1 below shows the human knee joint and its parts.

1.1 Role and functionality of cartilage

The function of the articular cartilage is to reduce compressive stresses between the articulating surfaces of the joint and to provide a bearing surface with an extremely low friction coefficient. Depending on our day-to-day activities, the stresses on the cartilage can go up to several times of our normal body weight. For example, during normal walking the knee joint can sometimes experience forces up to 7 times our body weight and it is obvious that these forces can go higher during performing activities like stair climbing, running or jumping (Mow et al., 1989). Other functions of the articular cartilage are to support and distribute loads and to provide lubrication within the joint (Boschetti, 2003).

1.2 Modes of lubrication

The knee joint is shown in figure 1.1 below. Lubrication within the synovial joint can take place in several ways. Goldsmith, (1996) suggests that lubrication takes place depending on various factors like stress levels, velocities, load distribution, etc. When relative velocities between the two opposing cartilage surfaces are low, the compressive

stresses are high and the loading period is long, it is known as boundary lubrication

(Goldsmith, 1996).

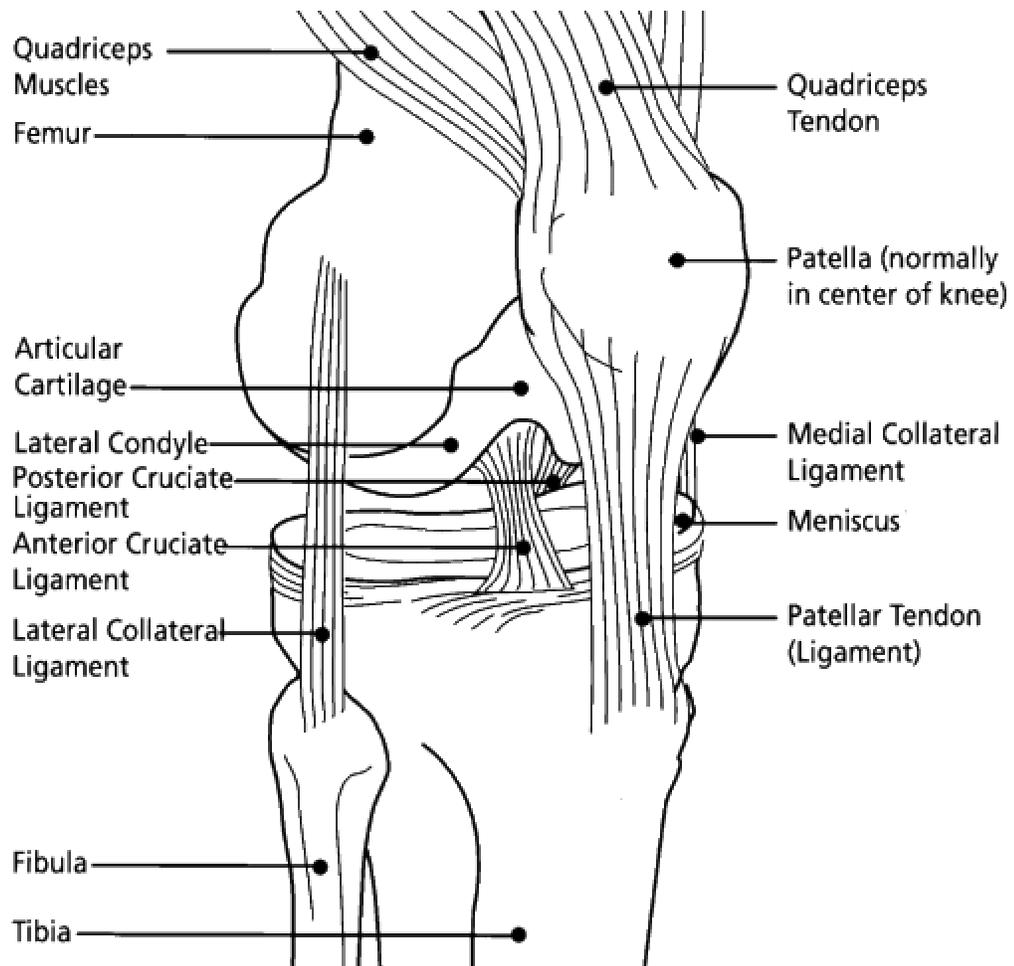


Figure 1.1: Human knee joint

Source: http://www.pueblo.gsa.gov/cic_text/health/qa-knee/Knee.gif

Figure 1.2 below shows the load distribution around the cartilage. One type of lubrication in a synovial joint depends on the relative velocities, stresses and the loading period. Fluid film lubrication has two broad types. If the two bearing surfaces are moving parallel to each other, a wedge of fluid is formed which supports the load. This is called squeeze film lubrication. The other kind is hydrodynamic lubrication where the two surfaces move perpendicularly towards each other.

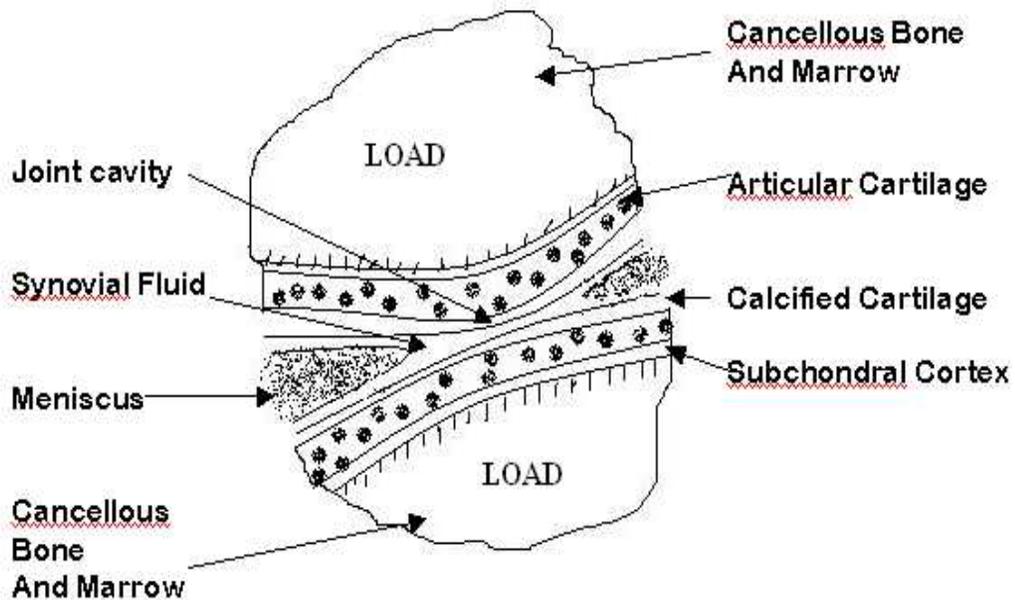


Figure 1.2: Articular cartilage: Load bearing region (Mow et al., 1986)

1.3 Disease of Synovial Joints

Arthritis is one of the most common medical problems and the number one cause of disability. The most common is osteoarthritis (OA), which is a form of degenerative joint disease, however there are many different kinds of arthritis. Based on a survey done in 2001 through the Behavioral Risk Factor Surveillance System, the estimated prevalence of the disease is about 69.9 million adults in the US (Bolen, 2001). It is a

condition affecting synovial joints and is characterized by cartilage loss and an accompanying periarticular bone response which can lead to the development of osteophytes and subchondral sclerosis (Ehrlich, 1978, Ehrlich, 1975). The cartilage loss in the joints results in eventual bone on bone contact causing pain and decreasing joint range of motion.

OA in general, adversely affects the load bearing, stabilizing, and lubrication functions of articular cartilage (Setton et al., 1999). The changes that take place as a result of the disease are surface fraying and splitting, appearance of gross ulcerations, disappearance of the full thickness surface, loosening of the collagen fibrils, loss of proteoglycans, increased water content, and increased chondrocyte activity (Martel-Pelletier, 1998, Inerot, 1978, Akizuki, 1986, Armstrong et al., 1982). Studies have also shown that OA causes an alteration in the mechanical properties of articular cartilage in tension, compression, and shear (Setton et al., 1999, Akizuki, 1986, Armstrong et al., 1982). Various factors such as obesity, injury, age, and genetics have been speculated to lead to the initiation of the disease. Once the tissue is damaged, subsequent and continuing use of it can lead to progression of the pathological process. Thus, emphasizing the importance of early diagnosis and prevention of the disease.

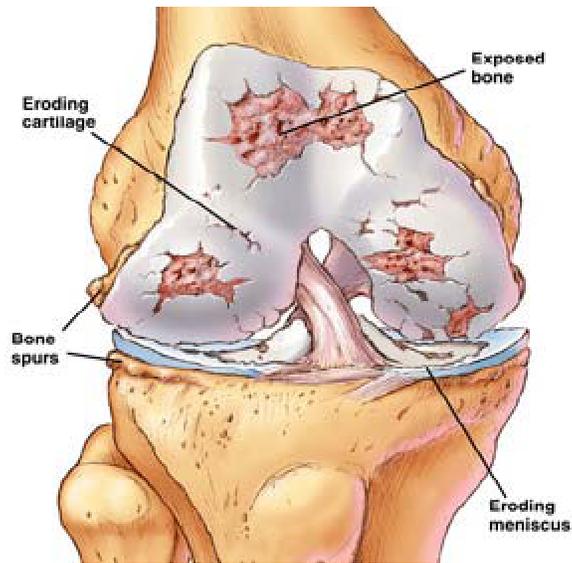


Figure 1.3: Osteoarthritis Knee Joint [zimer.com]

1.4 New trends in disease control of Synovial joints

Some new therapeutic options available of treatment of osteoarthritis can be listed as follows (Haq et al., 2003, Hochberg et al., 2000, Jordan et al., 2003, Altman et al., 2000):

Non-pharmacological treatment

- Education
- Social support
- Weight loss
- Exercise
- Orthotic devises
- Nutrients
- Herbal remedies
- Vitamins/minerals

Pharmacological treatment

- Paracetamol/Acetaminophen
- Non-steroidal anti-inflammatory drugs
- Cyclo-oxygenase-2 selective non-steroidal anti-inflammatory drugs
- Opioid analgesics
- Hormones
- Psychotropic drugs
- Symptomatic Slow Acting Drugs used for OA
- Topical NSAIDS
- Topical capsaicin

Non-invasive procedure

- Physiotherapy (physical therapy)
- Occupational therapy
- Laser
- Pulsed Electromagnetic field therapy
- Ultrasound
- Transcutaneous electrical nerve stimulation
- Intra-articular treatment

Invasive procedure

- Acupuncture
- Corticosteroids
- Hyaluronans
- Tidal irrigation

- Surgical
- Arthroscopy
- Osteomy
- Unicompartamental knee replacement
- Total knee replacement

The present work is limited to a new treatment for osteoarthritis of the knee known as intra-articular treatment. The substance is a mixture of modified hyaluronan molecules that can be injected into the joint to prevent bones from rubbing. It has been used in Europe at first, and has shown promise in tests as an alternative to some other treatments. It eventually works its way out of the body, but in one study, patients reported upto six months of relief. These kinds of treatments more commonly called Joint Fluid Therapy (Portyansky, 1997).

CHAPTER 2

BACKGROUND

Synovial joints have tough cartilage tissues which are ideal for withstanding heavy loads over a long period of time. The cartilages absorb shock arising out of sudden loads and distribute these loads across the joint. The structure of the joint makes the stresses across the bones more uniform. A cartilage consists of a cellular matrix, 20 % by weight, and liquid, 80 % by weight.

The bi-phasic structure of the cartilage consists of solid phase interspersed with a fluid phase. The alternating compressive and tensile stresses affect the mechanical behavior of the joint, which is dependent on the synovial fluid secretions that fill the matrix structure within the cartilage. At high rate of dynamic loading, cartilage is virtually incompressible, even though the shape of the matrix changes (Laasanen et al., 2003). Most of the fluid is free to move within the tissue (Kwan et al., 1984). Hence the solid phase bears the tensile stress and the liquid phase bears the compressive stress. In fact, nearly the interstitial synovial fluid supports 95% of applied load.

The mechanical property of the cartilage can be damaged during Osteoarthritis by damage to the solid phase, which means more fluid will be lost and load on the fluid will be shared by the solid which is obviously be a mechanical disadvantage (Lynn et al., 2004, Goldring et al., 2004, Goupille et al., 2003, Gao et al., 2004, Vanwanseele et al., 2003, Fowler, 2003, Guilak, 1999, Moseley, 2002, Llinas, 1993, Knirk et al., 1986).

Tremendous amount of research has been done and is still being done with respect to the mechanical and material properties of an articular cartilage. Kwan et al (1984) has given a mathematical theory for a linear bi-phasic model of an articular cartilage. The

properties of the cartilage were the outcome of an indentation experiment. The experiment included investigation of various parameters like stresses on the solid and the liquid phase, Young's modulus, permeability, Poisson's ratio, etc. (Goldsmith, 1996).

The analytical/mathematical models are useful and are the backgrounds of FE modeling but have their own limits to their applicability and capability. For all but the most narrowly defined problems, analytical solutions are not tractable, numerical solutions are only possible (Goldsmith, 1996).

Previously done experiments and analytical models give a strong base for the FE modeling of the articular cartilage. Biphasic modeling by Goldsmith (1996) gives various steps, which are recommended for the FE cartilage model, problem definition, meshing, boundary conditions, etc. Hence FE modeling has enabled problems to be modeled and parameters to be investigated that were not possible experimentally and analytically (Goldsmith, 1996).

Various experiments with the articular cartilage have been carried out in order to obtain the properties of the cartilage. Using these values, the FE models and simulations have been compared with realistic experiments and have given promising results. All this research is a motivation to step into the real world of problems and diseases related to the cartilage, out of which OA is the major one. Hence the main objective of this thesis is to mimic the fluid therapy procedure and is an attempt to optimize the same.

2.1 Assumptions

The literature search suggests the following common assumptions which have been used for FEM modeling.

- Articular cartilage needs to be modeled as a biphasic material, incorporating interstitial fluid flow, in order to predict the deformation and behavior (Goldsmith, 1996).
- An articular cartilage can be modeled as a flat geometry of uniform thickness. A comparison was made using a curved geometry and a flat geometry of an articular cartilage and both showed similar results (Goldsmith, 1996).
- The subchondral bone can be modeled as a rigid impermeable substrate. Modeling the bone as rigid and impermeable zone showed negligible effect in the experiments (Goldsmith, 1996).

2.2 Theoretical Modeling:

In modeling the cartilage, the parameters that are of importance are the aggregate modulus, Poisson's ratio and the permeability. The aggregate modulus can be expressed as:

$$H_A = E_S(1 - \nu_S) / (1 + \nu_S)(1 - 2\nu_S) \quad (1)$$

Where E_S is the Young's modulus and ν_S is the Poisson's ratio (Mow et al., 1991).

These are structural or mechanical properties, that are given as input into a software.

Darcy's law derives the permeability as:

$$k = Qh / A \Delta P \quad (2)$$

where Q is the volumetric flow rate, h is the permeation distance, A is the cross-sectional area of flow and ΔP is the applied pressure difference (Goldsmith, 1996).

Using an indentation experiment an expression for Young's modulus has been developed. During this experiment, the cartilage was modeled as single phase, taking the fluid flow effects into consideration (Goldsmith, 1996, Sokoloff, 1966, Hirsch, 1944).

$$E = P / 2.67w_o a \quad (3)$$

where P is the applied load, w_o is the depth of penetration and a is the radius of indenter.

2.3 Fluid Therapy and Hyaluronin

Treatment through viscosupplementation is a therapy that is carried out using a fluid immitating the joint fluid. This is commonly is known as Joint Fluid Therapy. Other common means of relief for arthritic patients are painkillers, physical therapy and exercise. Joint Fluid Therapy is used when all the other means fail. The artificial fluid is known as Hyaloronic acid is a pure form of Sodium Hyaluronate and it is injected directly into a knee joint using a syringe. A pure form of the fluid is either obtained from a natural source, which is rooster combs, or from an artificial source with the help of bacteria.

The aim of Fluid therapy is lubrication of the joint and to restore the mechanical properties of the cartilage for better shock absorption. As the cartilage is already in a damaged state, it is not able to retain the fluid for a long time. Hence such injections, depending on the condition of the patient, are usually given once a week or once in two weeks.

Joint Fluid therapy does not necessarily guarantee relief to all patients and does not stop the progress of the disease (Portyansky, 1997). For such patients the ultimate treatment would be surgery, which is expensive. The goal of this study is to optimize the Fluid Therapy and enable the treatment to work better for patients across the spectrum.

Potential mechanisms of action of intra-articular hyaluronans in treatment of osteoarthritis (Punzi, 2001) are as follows,

- Effects on joint mechanics
- Replacement of osteoarthritis synovial fluid with high molecular weight hyaluronans
- Increase in viscosity
- Pathophysiologic and structural effects
- Induction of hyaluronan synthesis
- Reduction of degradation of hyaluronan and other key components of cartilage and synovium
- Effects on the inflammatory process
- Control of cellular traffic between vascular and intestinal membranes at synovial membrane
- Effects on immune cell migration and function
- Effects on inflammatory cytokine production and function
- Direct analgesic effects

Table 2.1: Normal concentration ($\mu\text{g g}^{-1}$) of hyaluronan in various organs of human
(Laurent et al., 1986, Fraser, 1996, Laurent, 1996)

Organ or fluid	Man
Umbilical cord	4100
Synovial fluid	1400–3600
Dermis	200
Vitreous body	140–338
Lung	
Kidneys	
Renal Papillae	
Renal cortex	
Brain	35–115
Muscle	
Intestine	
Thoracic lymph	8.5–18
Liver	
Aqueous humour	0.3–2.2
Urine	0.1–0.3
Lumbar CSF	0.02–0.32
Plasma (serum)	0.01–0.1

CHAPTER 3

APPLICATION

3.1 Sysnoise

SYSNOISE is a commercial FEM software tool for solving common FEM problems using boundary element method (BEM), which is most useful in acoustics. It is capable of solving two-way fluid-structure interaction, using implementations of the finite element and boundary element methods focused on optimal solutions. Its domain can be a closed, open, or partially open, including homogeneous fluid or multiple fluids. A coupled structure can be wholly or partly connected to the fluid.

SYSNOISE utilizes numerical methods based on the direct and indirect boundary element method (DBEM and IBEM) and a pressure formulation for finite and infinite element modeling (FEM and I-FEM). A finite element model represents the elasticity of the fluid-loaded structure.

The basic equations used by SYSNOISE are derived from the compressible Navier-Stokes equation and the continuity equation as in other CFD codes. The equation below used as the main basis in this software (Sysnoise 5.6 manual).

$$\frac{1}{c_o^2} - \frac{\partial^2 p'}{\partial t^2} - \frac{\partial^2 p'}{\partial x_i \partial x_j} = \frac{\partial \dot{Q}}{\partial t} - \frac{\partial F_i}{\partial x_i} - \frac{\partial^2 T_{ij}}{\partial x_i \partial x_j} \quad (4)$$

where,

p' - is the pressure fluctuation,

\dot{Q} - the mass flow rate,

F_i - the external forces acting on the fluid and

T_{ij} - the Lighthill stress tensor containing momentum flux, thermal and viscous terms and c_0 - the speed of sound.

The equation below shows the form of continuity equation known as the exact continuity equation (Kinsler L. E., 2000).

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \bar{u}) = 0 \quad (5)$$

where,

- instantaneous density

\bar{u} - particle density in x-direction.

This is derived from the general equation of continuity used in fluid mechanics, which is shown below,

$$\left[\rho u x - \left(\rho u x + \frac{\partial(\rho u x)}{\partial x} dx \right) \right] dy dz = - \frac{\partial(\rho u x)}{\partial x} dV \quad (6)$$

This is in the x-direction and u is the particle velocity in x-direction and dV is the volume of the fluid element considered.

3.2 Finite element method

SYSNOISE solves the following system of equations during its finite element analysis and calculates a wide variety of results such as pressure and radiated sound power, velocities, etc.

$$\left[K + i\omega C - \omega^2 M \right] \{ p \} = \{ F_A \} \quad (7)$$

Where F_A is the vector of nodal forces, proportional to the normal velocity boundary conditions imposed on the faces of the mesh. The stiffness [K], damping [C] and mass [M] matrices are computed only once as they are independent of

the frequency. At each frequency, the system of equations is set up and solved to obtain the pressure distribution $\{p\}$ (Sysnoise 5.6 manual).

3.3 Fluid - Structure FEM coupling

Problems where the fluid-structure interaction is involved are referred coupled problems. This class of problems enables the calculation of the interaction of the structure and the medium in which it is immersed or which it encloses. Coupled models are also referred to as two-way coupling or Fluid-Structure coupling.

In a coupled analysis, the dynamic behavior of the structure is modeled using the Finite Element method while the fluid description can be based on the Finite Element method (with Infinite Elements if required) or the Direct or Indirect Boundary Element methods. All types of coupled problems are handled with the multi-model architecture of SYSNOISE.

This analysis procedure computes the response to excitation of a structure and the enclosed fluid. Two techniques are supported to represent both structural and fluid behavior:

- Physical coordinates (Direct Response)
- Modal coordinates (Superposition)

Excitations can be structural loads (forces) or acoustic loads (wave sources), taking into account any other boundary condition defined on the structure such as constrained, displacements, velocities, etc.

From these input data, the procedure computes both the structural response (displacements) and the potentials (nodal pressures, velocity and intensity) (Sysnoise 5.6 manual).

The calculation procedure sets up and solves a coupled system of equations involving both structural displacements and pressures as unknowns. For Physical coordinates, this system of equations takes the form:

$$\begin{bmatrix} K_S - \omega^2 M_S & C^t \\ C & K_F - \omega^2 M_F \end{bmatrix} \begin{Bmatrix} u \\ p \end{Bmatrix} = \begin{Bmatrix} F_S \\ F_A \end{Bmatrix} \quad (8)$$

where:

K_S and M_S Structural stiffness and mass matrices

C Geometrical coupling matrix

K_F and M_F fluid stiffness and mass matrices

F_S and F_A Structural and acoustic load vectors

u Vector of nodal displacements

p Vector of nodal pressures

The FEM Coupled Analysis method benefits from the multi-model architecture and the coupling is obtained by linking two separate models by a Fluid-Structure link:

- a FEM Structure model
- a FEM Fluid model

The fluid mesh and the structural mesh must be compatible along their common interface.

The FEM Structure model must contain the following data, for Physical coordinates:

- Analysis option
- Structural mesh (Import Mesh)
- Structural geometrical properties
- Structural material properties
- Structural boundary conditions (displacements and loads)

The FEM Fluid model requires the following data, for Physical coordinates:

- Analysis option
- Fluid mesh (Import Mesh)
- Fluid material properties
- Pressure and Velocity boundary conditions

The FEM Coupled Analysis procedure calculates and stores data in both model databases:

In the FEM Fluid model database:

- Potentials: pressure, velocity and intensity values on the nodes of the FEM mesh
- Results: pressure, velocity and intensity values at field points

In the FEM Structure model database:

- Structural displacements on the nodes of the structural FEM mesh (Sysnoise 5.6 manual).

CHAPTER 4

PREPROCESSING AND MESH GENERATION – TYPICAL CASES

Here, four different cases of arthritis have been simulated for four different stages in an arthritic knee under various conditions. A comparison has been made, giving a clear idea of scope to improve the arthritis fluid therapy.

As it can be seen, the Figure 4.1 below shows case 1, which has been modeled as the most primary stage of arthritis. This is a stage where the cartilage has just started to degrade or damage and develops cracks or openings shown in Figure 4.6. It is at this stage when the cartilage loses moisture and starts to form cracks or openings mostly in the dried-up areas. During modeling this stage, an opening has been created in the x-direction of the axis. This kind of opening is common in all the stages but there are other differences which have been explained below.

Table 4.1: Description of cases

Case No.	Cartilage Condition	Figure No.
1.	Preliminary stage of disease. 10% damage. Refers to the initial stages where Fluid Therapy is most effective	4.1
2.	Refers to secondary stage of disease. Deformation seen on 50% of the layer which supports the Femur	4.2
3.	Final stage of disease. Fluid Therapy is least effective. Only source relief beyond Fluid Therapy is expensive knee replacement surgery.	4.3
4.	A test case. Cartilage changes shape due to disease. Effective treatment can be done after comparing results with previous cases.	4.4

Case 2 has been modeled similar to case 1. The difference being that this has been modeled at secondary stage of the disease. This can be seen clearly from the Figure 4.2. In case 2, it can be seen that the cartilage has more deformation than that in case 1. Now since there is more deformation, the fluid will ooze out with a greater velocity than that in the previous case.

Case 3 is the tertiary stage or a stage where the cartilage has degenerated more than that in case 2. This is shown in Figure 4.3. In case 2, there is only one area of deformation and in case 3 there are two deformed areas, one enclosed in another. At this stage the synovial fluid voids the cartilage space at a quicker rate than in case 2 and case 3.

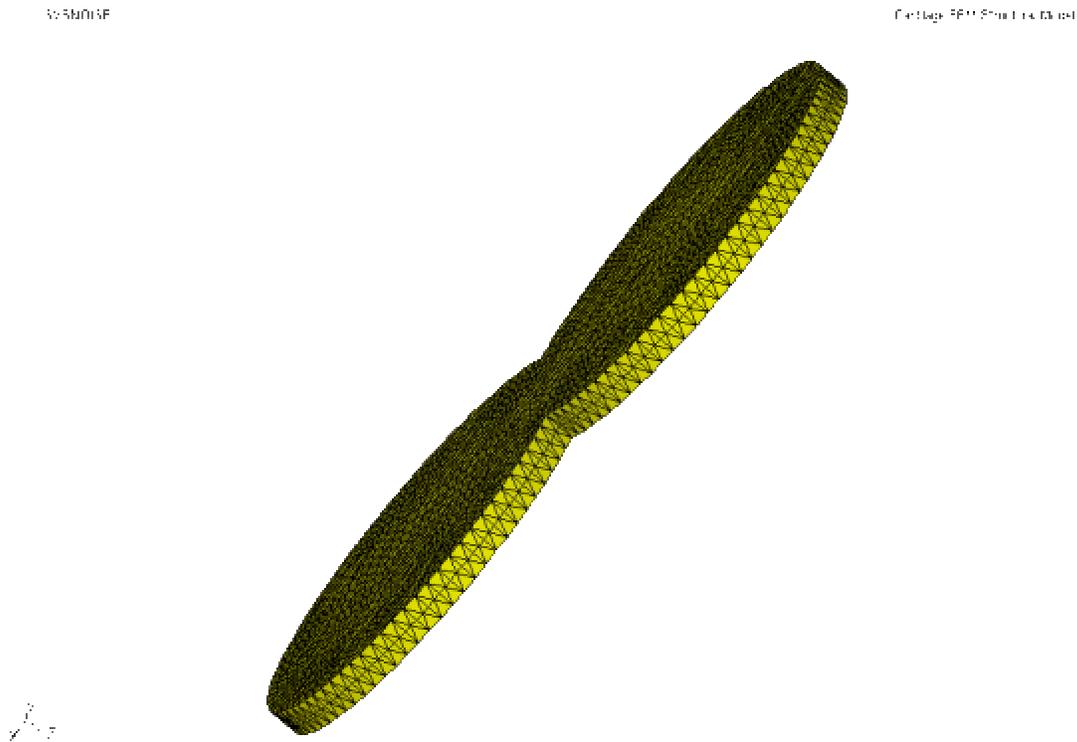


Figure 4.1: Case1 model mesh

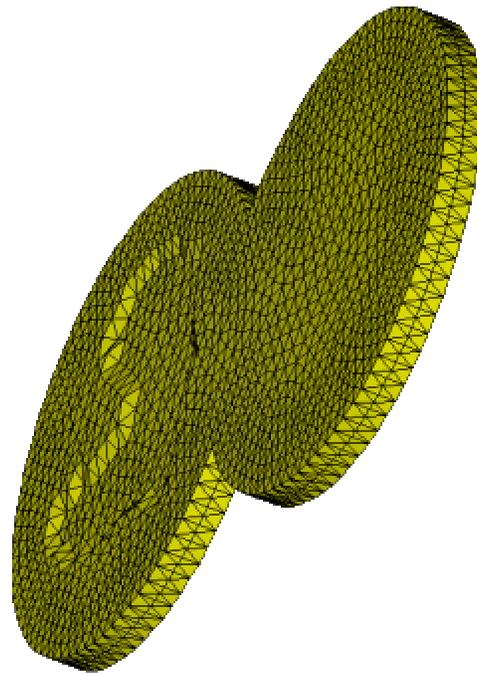


Figure 4.2: Case2 model mesh

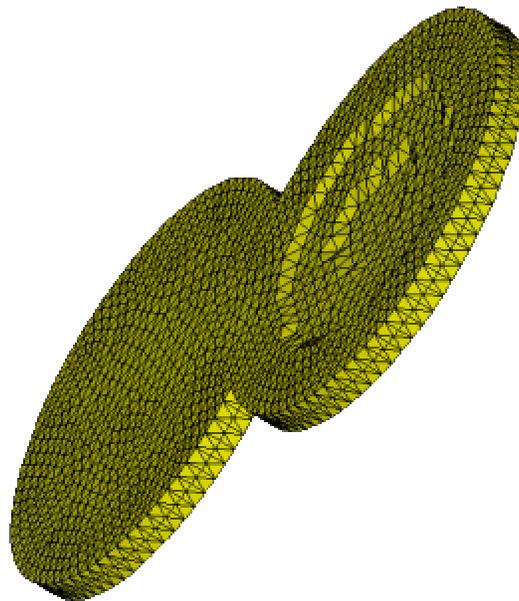


Figure 4.3: Case 3 model mesh

The cartilage is made up of a thin, viscoelastic material, which does not possibly have a definite shape. Hence, case 4, shown in Figure 4.4, has been modeled as a test model where the cartilage has a slightly different shape and deformation than in the above cases. This makes it uneven and can be used for comparison as if a 2nd sample of the cartilage. With the results, one will be able to decide to which of the above stages its behavior is closest to and this in-turn would decide the level of treatment required.

Dimension of the fluid and the solid model combined together are given below.

Length = 48.5mm.

Breadth = 26mm.

Depth = 2mm.

All the cartilage (solid) models have around 2770 nodes and 5530 tri-elements and the fluid model around 3460 elements and around 12000 tri-elements. Each tri-element is defined by three nodes by any software. The fluid volume is approximately 20000 mm^3 or 20cc, that is the volume of the syringe they inject into the cartilage during fluid therapy.

The modeling can be done using any commercial CAD software and in this case CATIA V5 has been used. SYSNOISE requires that both, the fluid mesh and the solid mesh, are to aligned; that is, the node alignment between the inside of the shell mesh and on the outside of the solid mesh. This kind of meshing is achieved using the help of HYPERMESH.

Pressure (kPa)

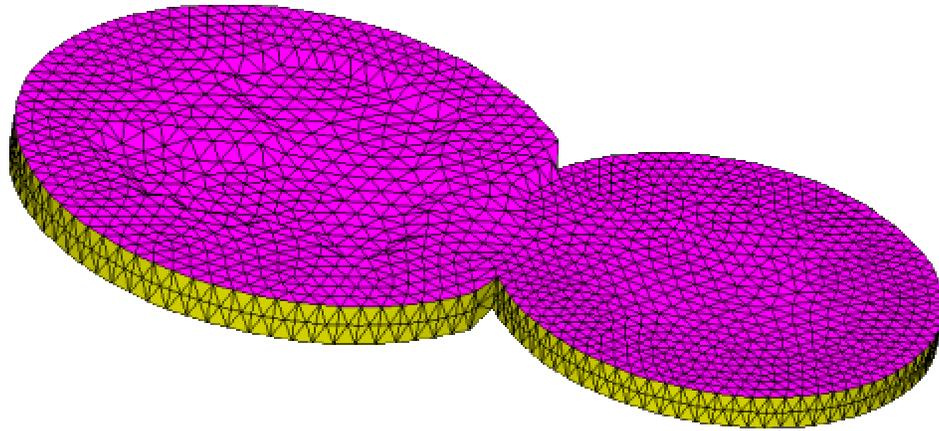


Figure 4.4: Case 4 model mesh

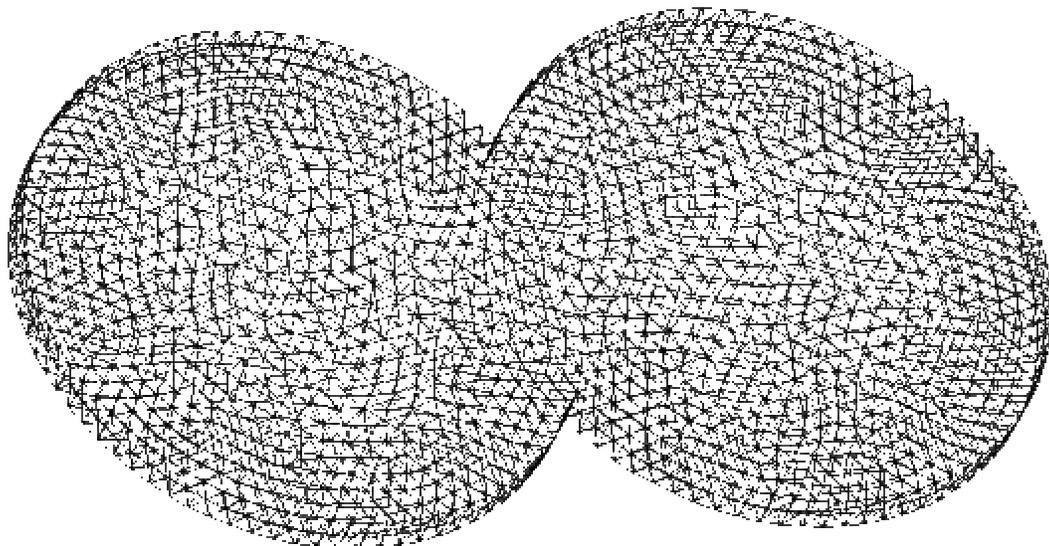


Figure 4.5: Wire mesh

At first, the meshes are imported. Before importing, SYSNOISE gives us an option to select either FEM Structure or FEM Fluid. FEM Structure and FEM Fluid options have been used for the shell and the fluid meshes respectively. After selecting the appropriate options and importing the meshes, the material properties were defined for the meshes so as to define the shell mesh as the cartilage and the fluid mesh as the cartilage or Synovial fluid.

The main aim of this research is to perform a coupled analysis or carry out the fluid-structure interaction, to simulate the knee dynamics, for which the two meshes have to be linked. This simulation can be used to validate or verify various parameters and further research can be performed on these parameters, before applying them to a realistic case.

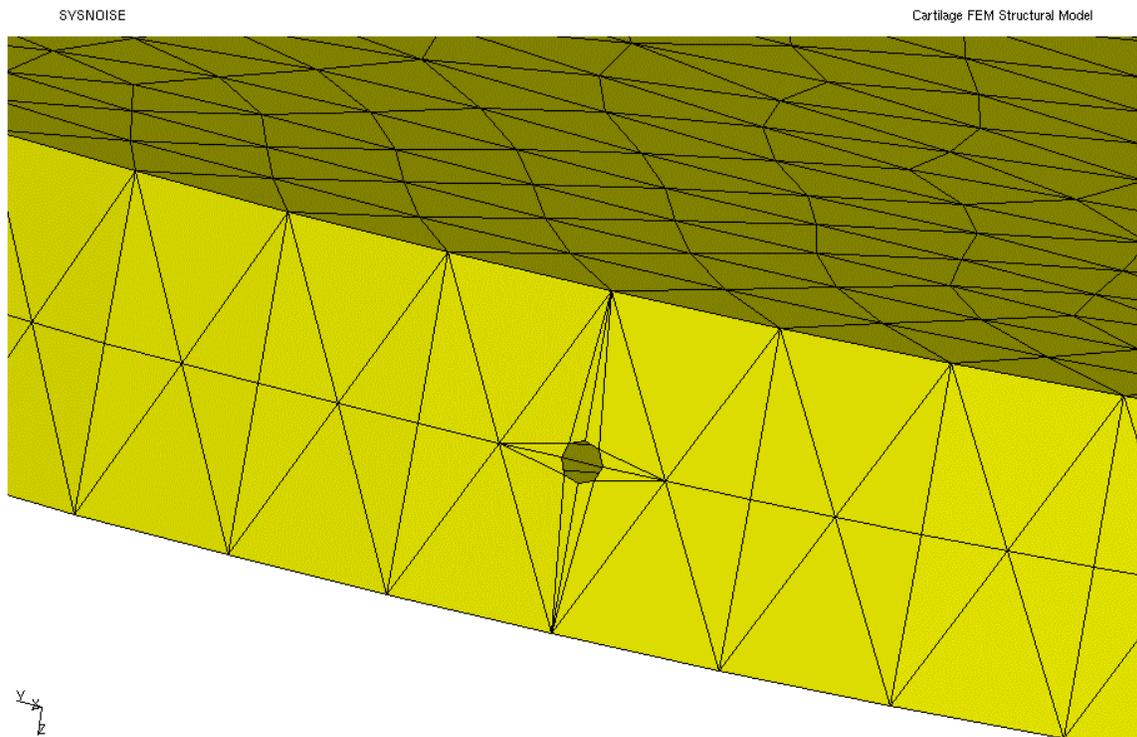


Figure 4.6: Cartilage opening

In SYSNOISE, sets comprising of the coupling elements and nodes is formed in each of the meshes. In this case the structural mesh is linked with the fluid mesh excluding the part of the fluid mesh corresponding to the opening in the solid mesh. This is because there is no material available for the coupling. Hence, set operations are carried out in the fluid mesh. This is shown in the Figure 4.7 below. The center red or the dark colored part shows the area of the fluid model which does not participate in the coupling, as there is no material on the shell or the cartilage model to allow coupling.

Figure 4.8 shows the coupled model which is ready for analysis. The cartilage is slightly wetted by the synovial fluid. Therefore the fluid model is represented as though fluid is permeated through the cartilage. The color codes used make it visible.

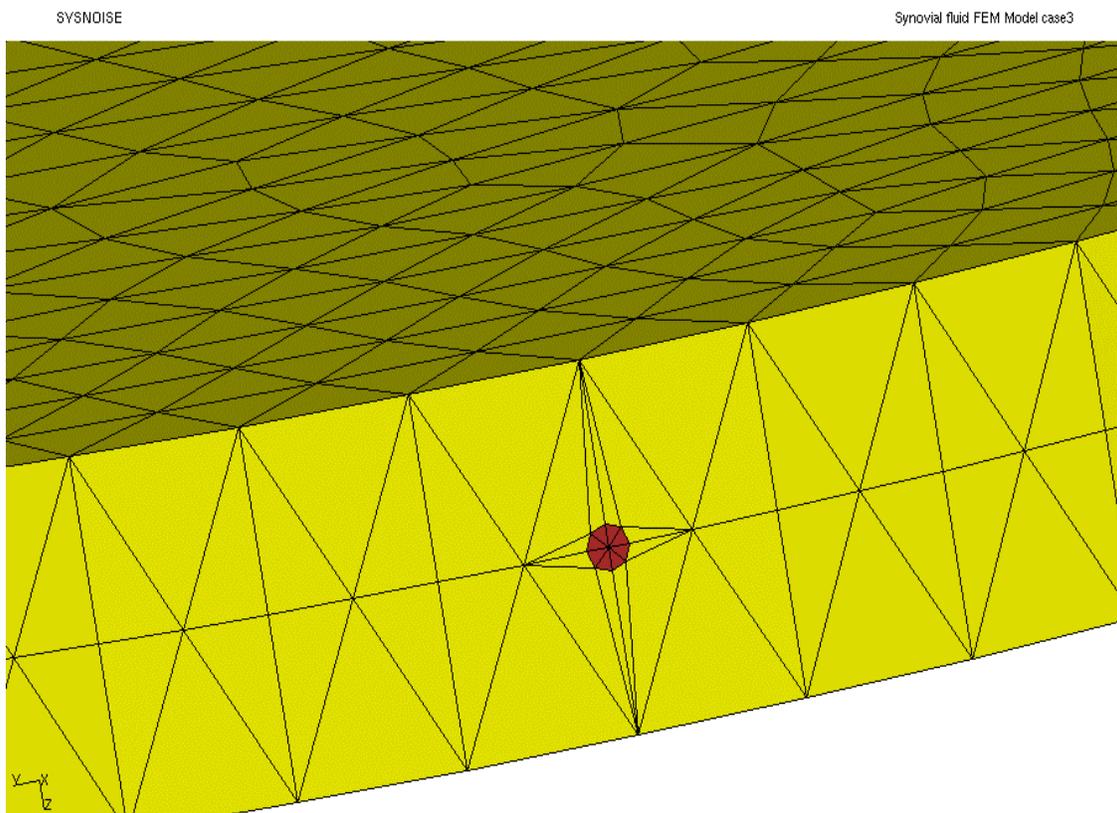
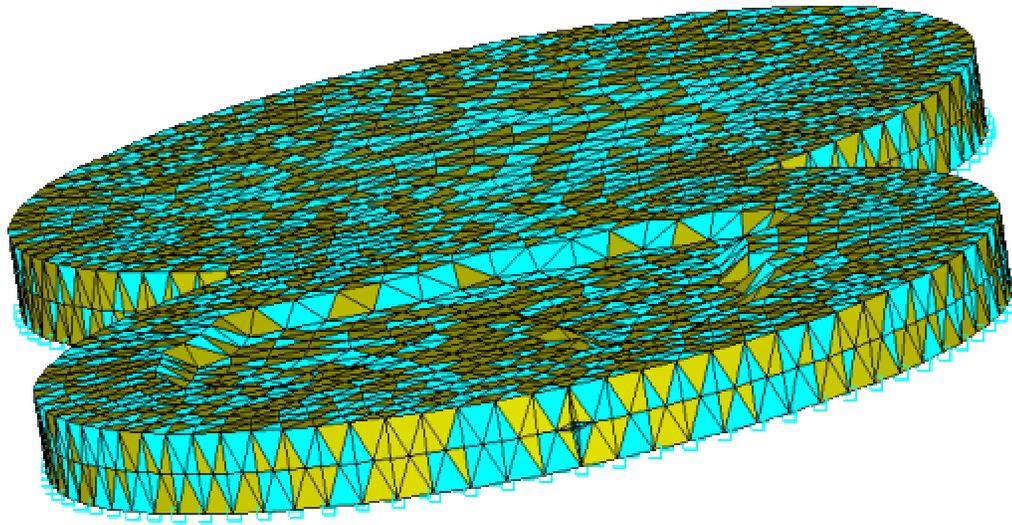


Figure 4.7: Coupling sets

■ [E] synchro flow (MATERIAL)



12

Figure 4.8: FSI

The base of the cartilage has been constrained, which can be regarded as the Tibia-the bone being situated below the cartilage. The pressure on the cartilage is applied by the Femur- the bone connecting the hips to the knee (the bone that supports the thigh). Displacement constraints are applied on the bottom surface and the load applied on the top flat surface is in a direction normal to the surface as shown in the following figures, 4.9 and 4.10. The pressure is applied by both, the femur and tibia and the pressure applied is distributed on the top and the bottom surfaces of the cartilage. But since the proposed model in this work is assumed to be flat, there will not be any variation in the pressure distribution.

[M] Displacement (BC)

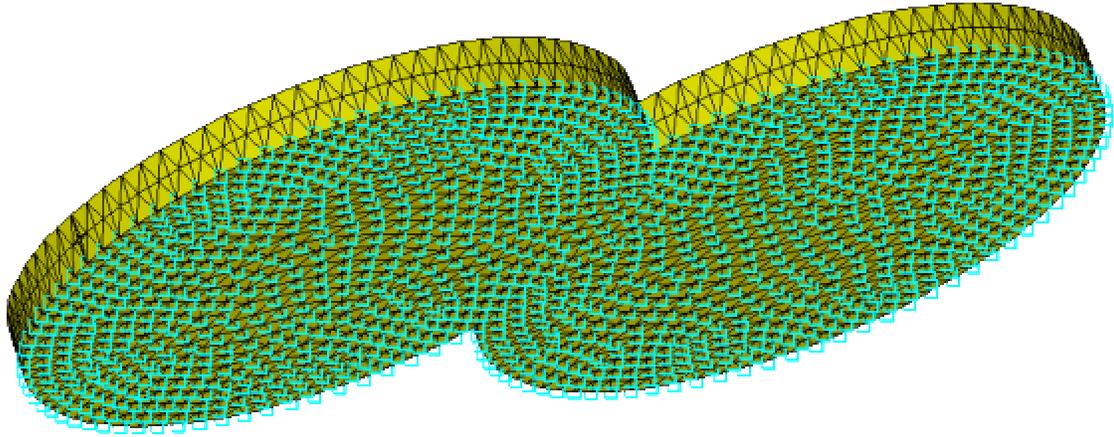


Figure 4.9: Displacement BCs

[E] Pressure (BC)

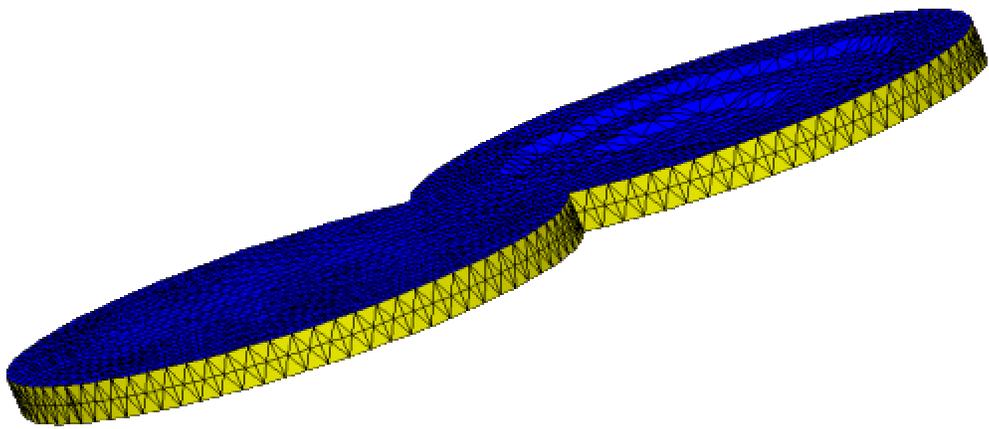


Figure 4.10: Pressure BC

CHAPTER5

RESULTS AND DISCUSSION

5.1 Simulation Results

The results of the finite element analysis using SYSNOISE have been presented in the subsequent paragraphs. Displacements, pressure contours and velocity color maps have been represented with respect to the onset of the disease

The figure below shows the picture of the deformed cartilage. The flat surface in the middle shows that the two bones bang into each other as the fluid displaces out of the cartilage.

In case there was no opening or damage, the fluid would have supported the load on the cartilage and prevented the two bones from coming on to contact and hence would have protected the thin cartilage. As discussed above, it is the fluid which bears the load and the compressive stress and the cartilage keeps the fluid intact or in position. Due to this disease, the fluid loses its position and leads to destruction (Laasanen et al., 2003).

SYS1.2.3E
Model Mesh [1]
[D]: Displacement

Cartilage FEM Structural Model

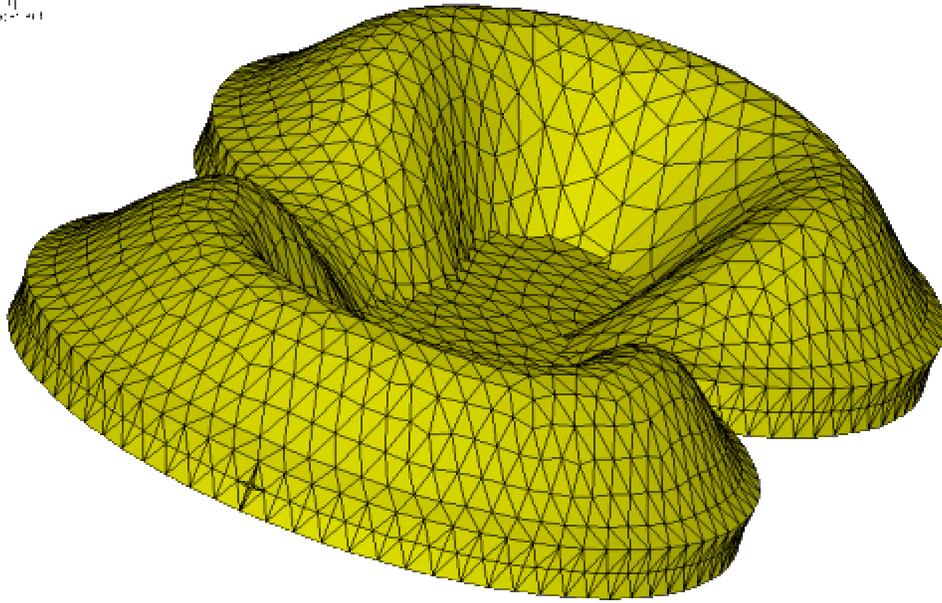


Figure 5.1: Cartilage deformation 1

SYSNOISE
Model Mesh [1]
[D]: Displacement

Cartilage FEM Structural Model

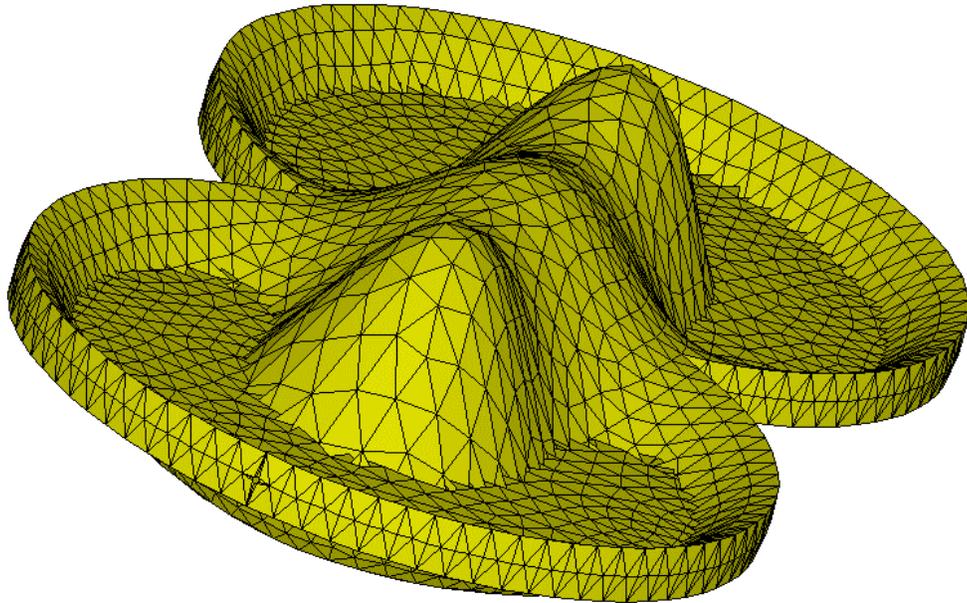


Figure 5.2: Cartilage Deformation 2

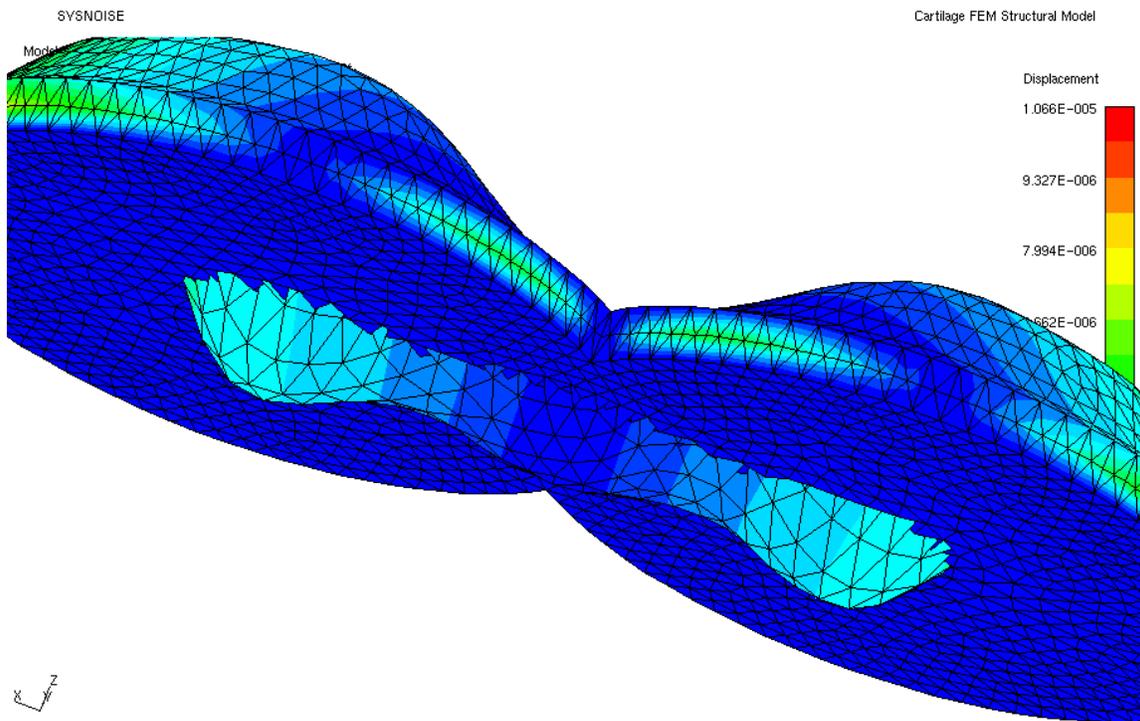


Figure 5.3: Cartilage Deformation (bottom)

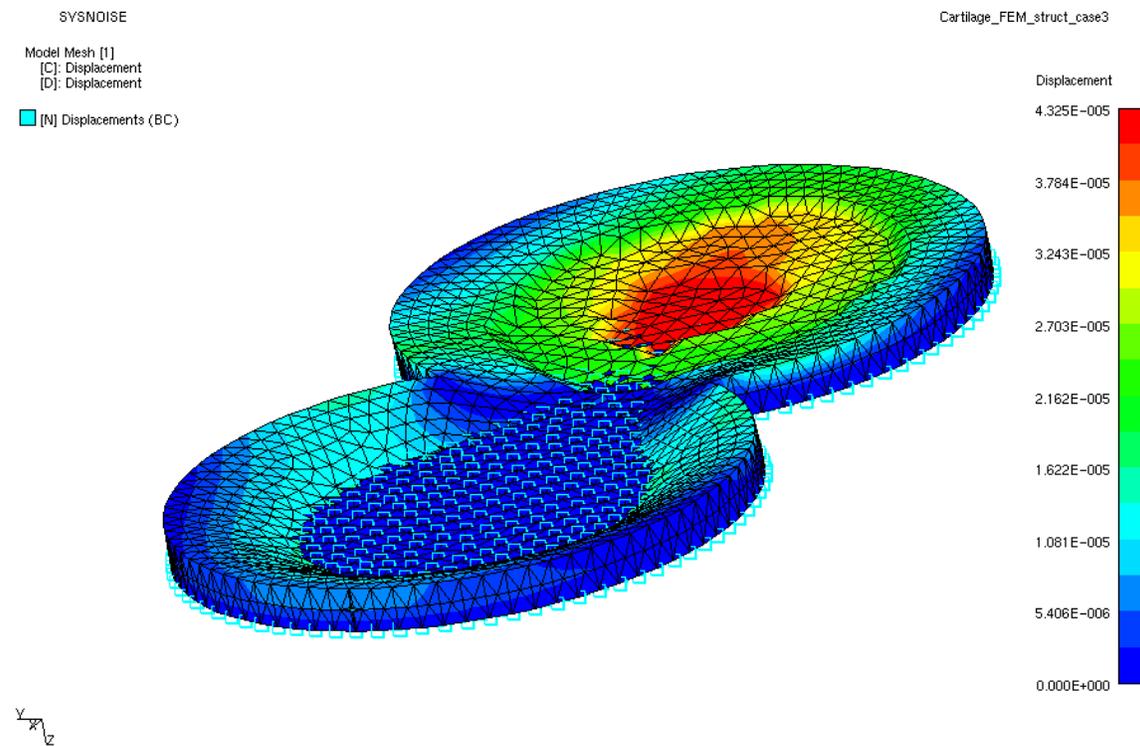


Figure 5.4: Displacement color map

The figure above shows the results from the simulation that shows displacement of the cartilage. Area of maximum displacement is consistent with the damaged zone of the cartilage. Most of the load comes on this area even though the pressure applied on the cartilage is even on the whole of the top surface. This correlates with the real life behavior of the damaged cartilage.

The figure below shows the velocity color map of the fluid model after the load has been applied. The values shown are in in/sec. It was previously mentioned that the opening on the cartilage model was on the x-direction of the cartilage. It is evident from the figure that the velocity at the opening is at a minimum while the maximum velocity is at a different area. This shows that, despite the cartilage being cracked, the highly viscous fluid can still bear the load but is slowly oozed out instead of loosing in a steady stream of gush quickly.

SYSNOISE
Model Mesh [1]
[C]: Velocity

Synovial fluid FEM model case4

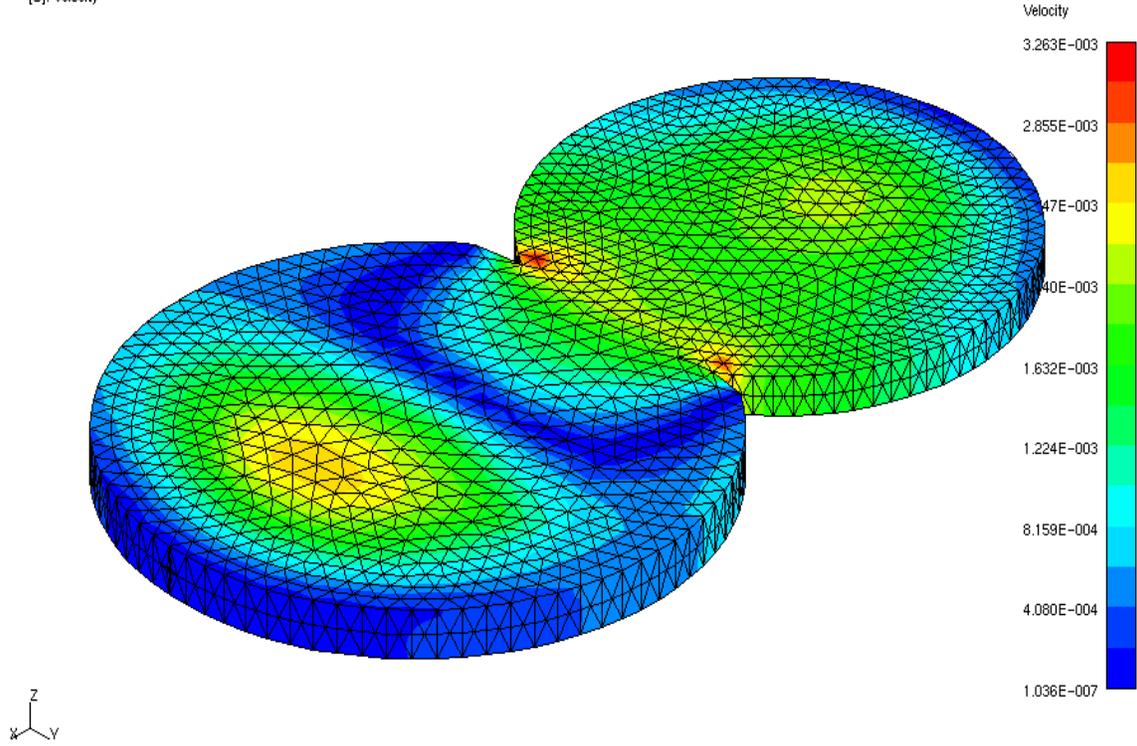


Figure 5.5: Fluid velocity color map case 4

5.2 Interpretation of results

All of the models considered in the current study have been subjected to 4 kinds of activity levels humans perform in their day-to-day life. The four cases are slow walking, fast or brisk walking, jogging and running. Then the approximate time taken for each activity for one step or one human stride has been considered. According to a study, published in the Road Engineering Journal, conducted in 1997 by Transsafety Inc., an average human walking speed is around 4 feet/sec. Previous research shows that the cartilage experience around $0.75 \text{ MN/m}^2 - 1 \text{ MN/m}^2$ (Goldsmith, 1996). Using these values as basis for the force response, the graph below has been generated and an average peak force of 150 pounds has been considered for this simulation. All units are in lbf-in-sec, for the sake of simplicity. Here is a general Force Vs Time chart which has been used in all the cases to make it feasible to compare results.

Force Vs Time

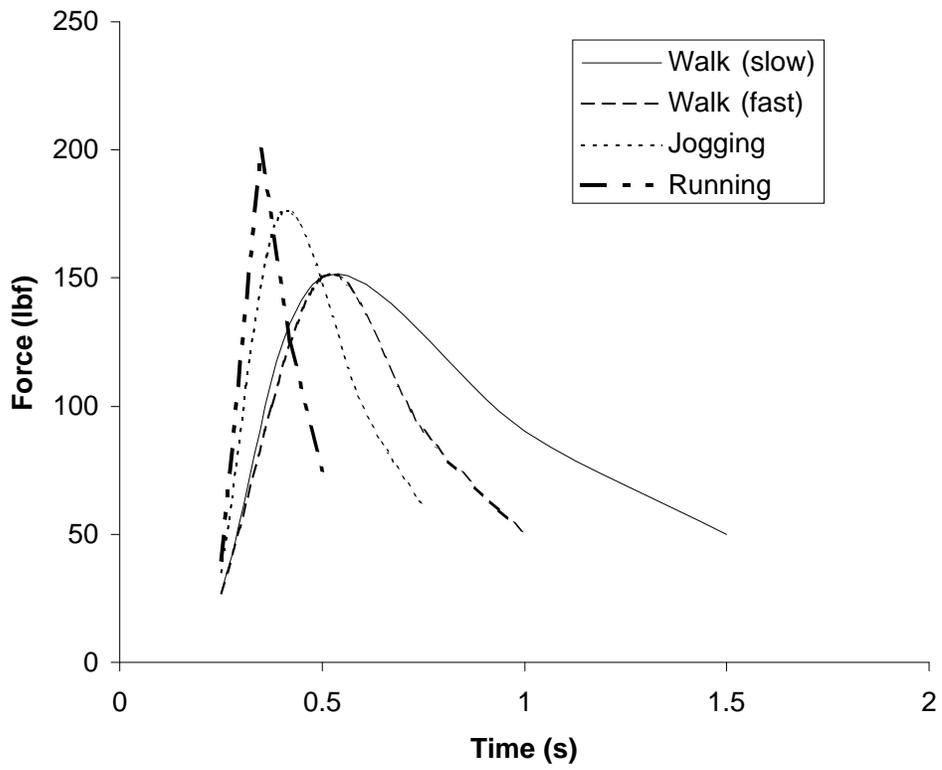


Figure 5.6: Force Vs Time chart

5.3 Case Study

Case 1

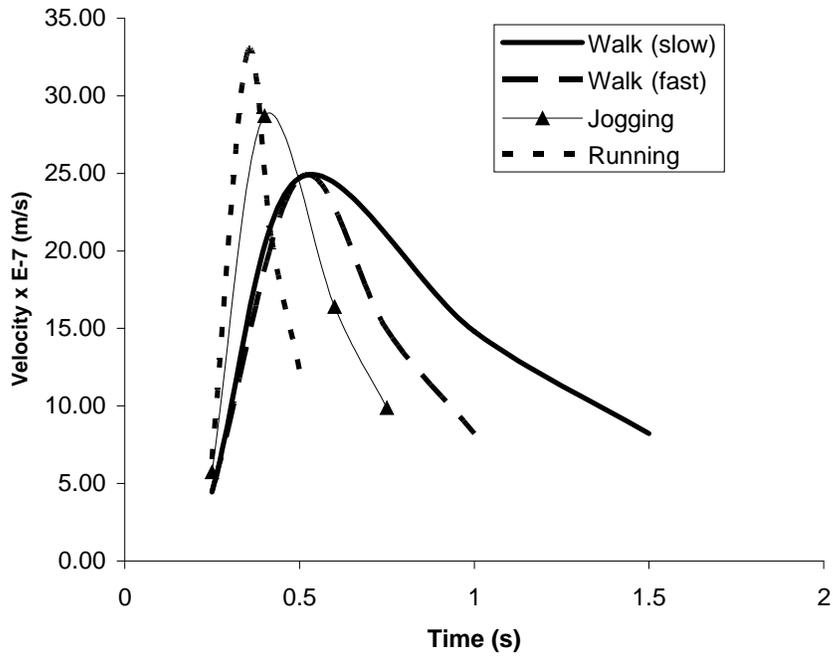


Figure 5.7: Time-Velocity Chart of Case 1

The chart above shows results obtained for the primary stages of the disease, for the four activities that were considered. The results above show the velocity with which the fluid exits the cartilage. It can be seen that the peak velocity for walking at this stage has a lower much value than that for running or jogging. Hence this is in agreement with the statement in the article by Goldsmith, 1996, which says that activities like jumping or running can pressurize the cartilage much more than simple walking. A simple calculation is performed to determine how long the medicine will last under the current situation.

Calculation

$$\text{Volume of fluid (}\mathbf{U}\text{)} = 20\text{cc} = 1.22047 \text{ in}^3$$

$$\text{Area of opening/crack in cartilage (}\mathbf{a}\text{)} = 7.73 \times 10^{-3} \text{ in}^2$$

$$\text{Velocity of synovial fluid coming out of the cartilage (}\mathbf{v}\text{)} = 5.85 \times 10^{-5} \text{ in/s}$$

$$\text{Volume Velocity} = \mathbf{v} \times \mathbf{a} = 4.52205 \times 10^{-7}$$

$$\text{Time for the entire fluid to void} = \frac{\mathbf{U}}{\mathbf{a} \times \mathbf{v}} = 2698930.795 \text{ s}$$

$$= 31 \text{ days.}$$

Case 2

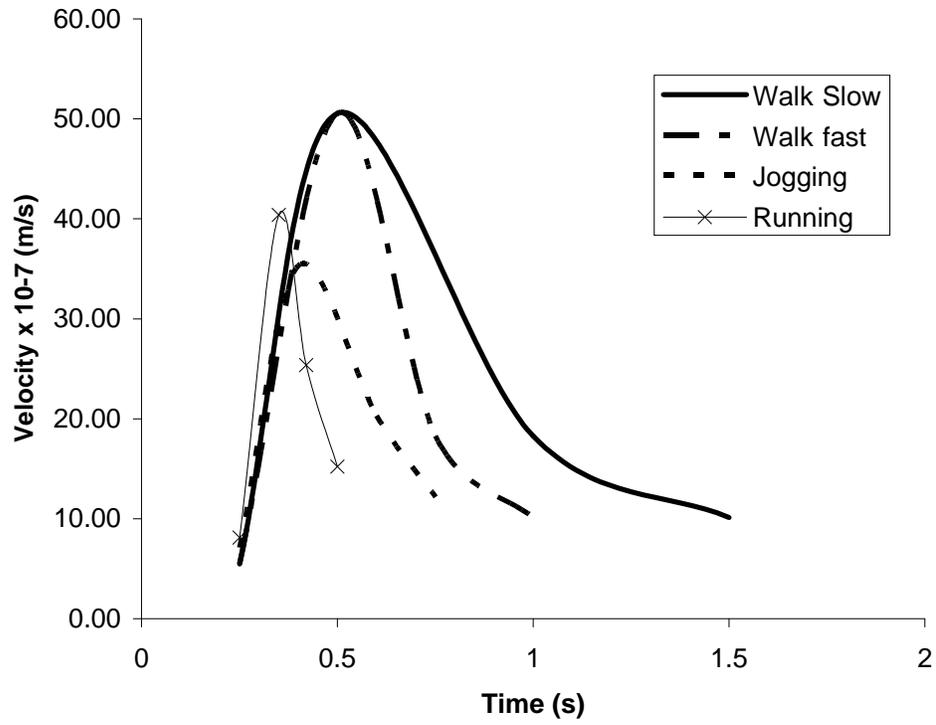


Figure 5.8: Time-Velocity Chart for Case 2

A similar kind of graph for the next stage of the disease or case 2. As mentioned above this stage is a secondary stage of the disease. Here the cartilage deformation is much more than that in case 1. In this stage, it can be observed that the peak velocity for the latter activities, running and jogging, is lower than that in simple walking but the overall velocity is higher in the latter cases. One of the possibilities for such abnormal/unexpected behavior can be that since the time for one step of running is much less than that for walking, the fluid does not get enough time to reach its peak value but because of inertial effects the fluid continues to flow at a higher average velocity.

Calculation

$$\text{Volume of fluid } (\mathbf{U}) = 20\text{cc} = 1.22047 \text{ in}^3$$

$$\text{Area of opening/crack in cartilage } (\mathbf{a}) = 7.73 \times 10^{-3} \text{ in}^2$$

$$\text{Velocity of synovial fluid coming out of the cartilage } (\mathbf{v}) = 8.19 \times 10^{-5} \text{ in/s}$$

$$\text{Volume Velocity} = \mathbf{v} \times \mathbf{a} = 6.33087 \times 10^{-7}$$

$$\text{Time for the entire fluid to void} = \frac{\mathbf{U}}{\mathbf{a} \times \mathbf{v}} = 1927807.71 \text{ s}$$

$$= 22 \text{ days.}$$

Case 3

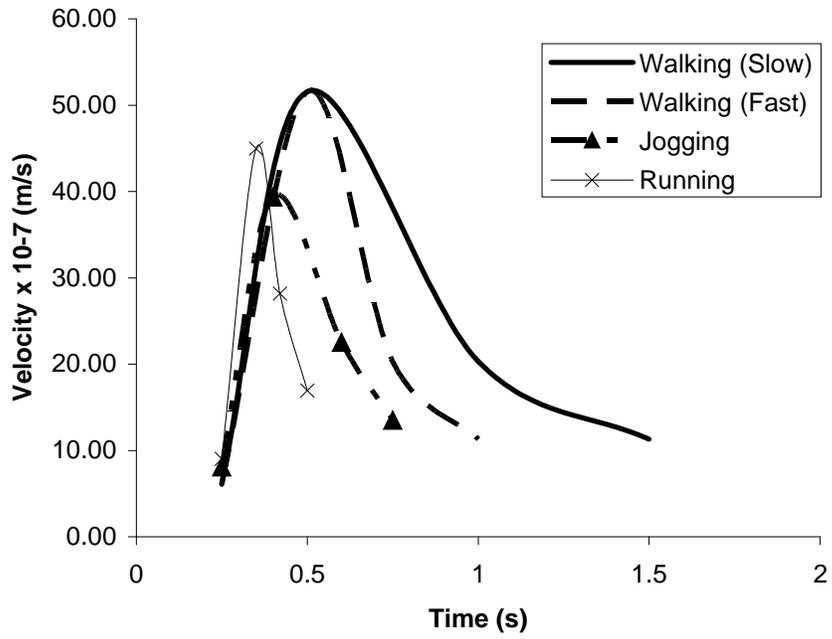


Figure 5.9: Time-Velocity Chart for Case 3

The above graph for Case 3 shows similar results as those of Case 2 but the velocities in case of the last two activities (jogging and running) are higher than those in case two. Again since this is a higher stage of the disease, the calculation below shows compatible results. Another interesting point about the graph above is that the peak velocities of Walking (fast) and running are higher than walking (slow) and jogging respectively. This is more prominent in the latter cases. This might simply be because of high pressure in a limited time. But the time might not be sufficient enough for the velocity to reach high values in the latter activities, as mentioned above.

Calculation

$$\text{Volume of fluid (U)} = 20\text{cc} = 1.22047 \text{ in}^3$$

$$\text{Area of opening/crack in cartilage (a)} = 7.73 \times 10^{-3} \text{ in}^2$$

$$\text{Velocity of synovial fluid coming out of the cartilage (v)} = 8.89 \times 10^{-5} \text{ in/s}$$

$$\text{Volume Velocity} = v \times a = 6.87197 \times 10^{-7}$$

$$\text{Time for the entire fluid to void} = \frac{U}{a \times v} = 1776011.82 \text{ s}$$

$$= 20 \text{ days}$$

Case 4

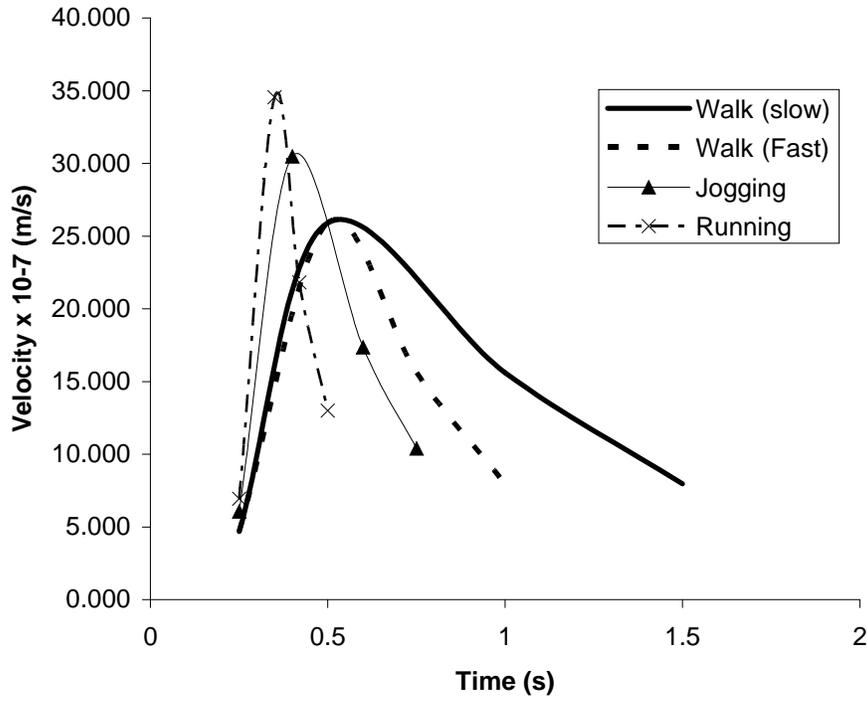


Figure 5.10: Time-Velocity Chart for Case 4

The figure above for Case 4 shows similar results as that of Case 1 but the only difference in this one is higher velocities of the fluid coming out of the cartilage. Performing activities like running take lesser time than walking. Calculation below will decide the better stage of the disease.

Calculation

$$\text{Volume of fluid } (\mathbf{U}) = 20\text{cc} = 1.22047 \text{ in}^3$$

$$\text{Area of opening/crack in cartilage } (\mathbf{a}) = 7.73 \times 10^{-3} \text{ in}^2$$

$$\text{Velocity of synovial fluid coming out of the cartilage } (\mathbf{v}) = 6.12 \times 10^{-5} \text{ in/s}$$

$$\text{Volume Velocity} = \mathbf{v} \times \mathbf{a} = 4.73076 \times 10^{-7}$$

$$\text{Time for the entire fluid to void} = \frac{\mathbf{U}}{\mathbf{a} \times \mathbf{v}} = 2579860.318 \text{ s}$$

$$= 29 \text{ days}$$

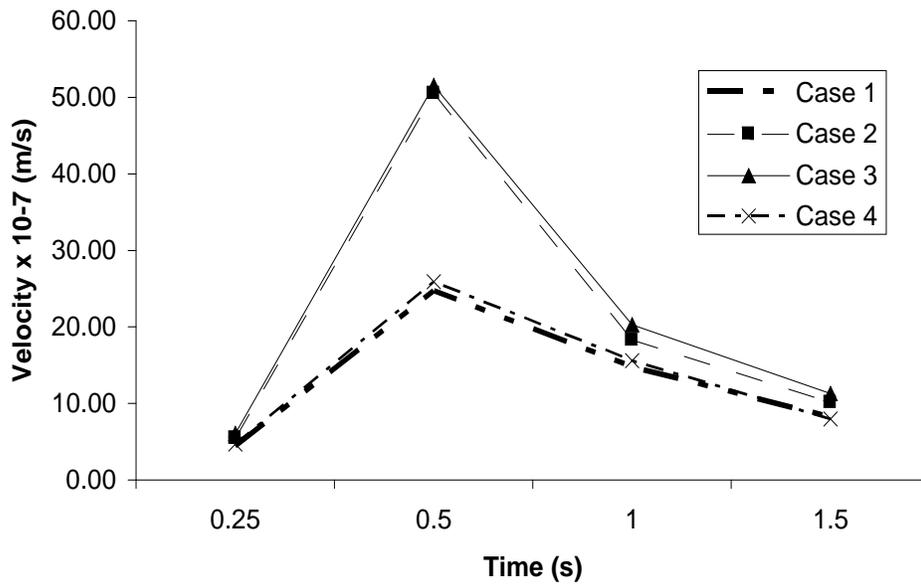


Figure 5.11: Time-Velocity for Walk (slow) Comparison

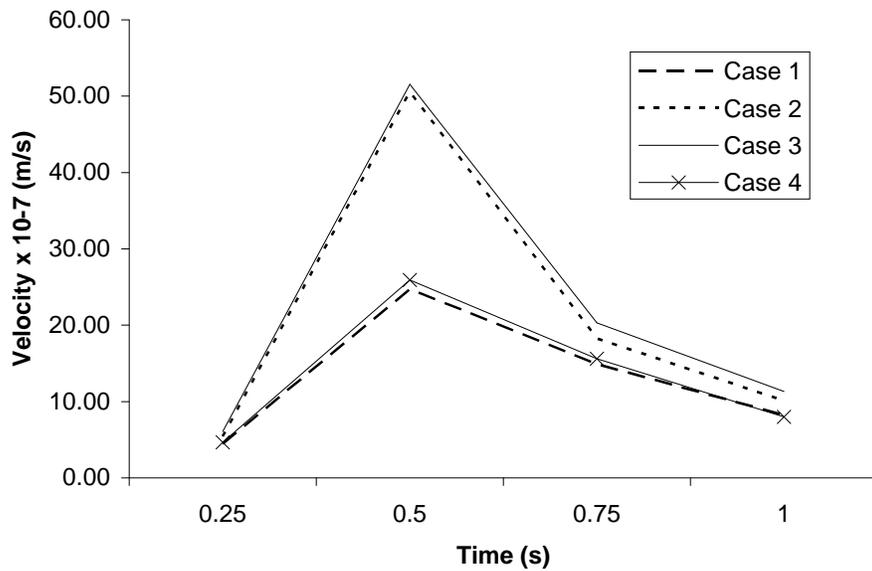


Figure 5.12: Time-Velocity Chart for Walk (fast) Comparison

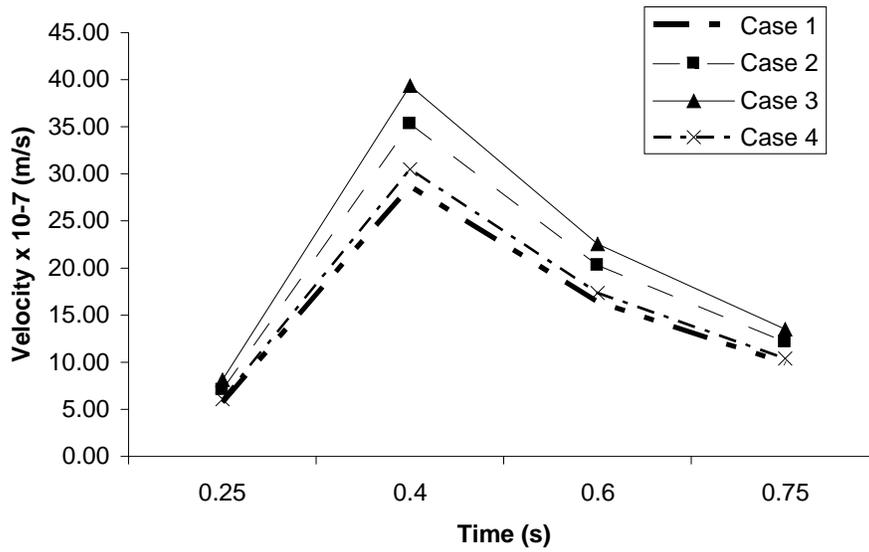


Figure 5.13: Time-Velocity Chart for Jogging Comparison

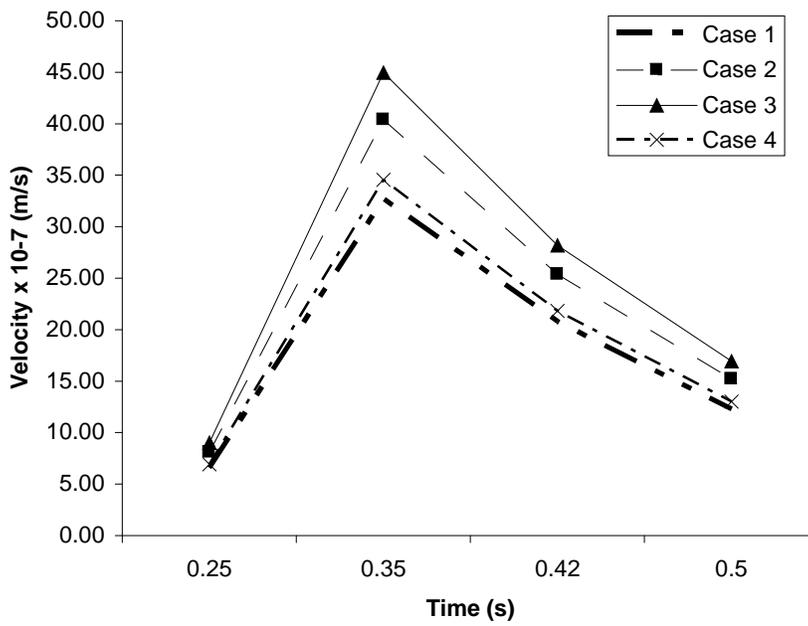


Figure 5.14: Time-Velocity Chart for Running Comparison

Charts 5.11 to 5.14 compare each activity for each case. Activities like running can apply several times of force more than that in case of activities like walking (Goldsmith, 1996). It can be seen that in the initial stages of the disease the velocity of the fluid is less than that in the latter stages. This is a good point which proves the simulation. Be it brisk walking or normal walking, the results seem to be quite similar the only difference being that the velocities for the activity are slightly higher. Case 4 and Case 1 show similar results. Case 4 can be considered as a test model with the help of which the stage of the disease can be decided just by comparing the results.

In the graphs 5.11 and 5.12 for case 2 and case 3, it can be seen that for the latter two activities the cartilage show lower fluid velocities than that for cases 1 and 4. In spite of this abnormal behavior, the average velocity was much higher in case 2 and much more higher in case 3. In this graph above it is clear that the velocities show feasible results. The velocities for jogging and running are still higher than that for walking.

The graphs 5.13 and 5.14 above are similar, but the difference being the time. The velocity values also seem much higher than that in case of the jogging activity. In case of the last two activities (jogging and running), it can be seen that case 1 and case 4 show similarities. Again case 4 can be regarded as a test case where the cartilage behavior is similar to that in case 1. This can give scope for further research.

The chart below in Fig. 5.15 shows a detailed comparison of the average velocity (in m/s) and the number of days the fluid takes to void the synovial space in the joint, for each case.

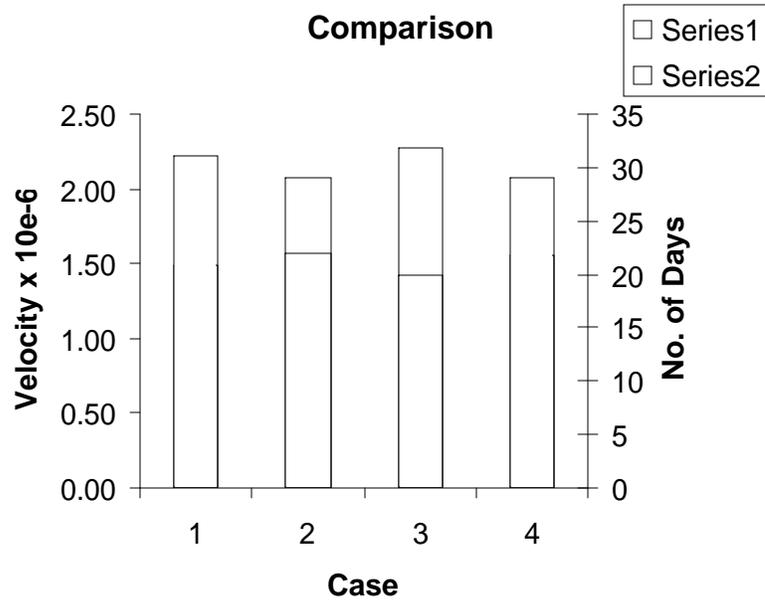


Figure 5.15: Comparison bar chart

Table 5.1: Comparison Chart

Velocity	Case	Days
1.49	1	31
2.08	2	22
2.27	3	20
1.56	4	29

CHAPTER 6

CLINICAL RELEVANCE

From various resources it has been known that until now OA has no specific cure. Treatments for OA are either non-pharmacological or pharmacological and others are surgical. Surgical treatments mainly come into picture when the rest of the two kinds of treatments completely fail. The non-pharmacological or pharmacological treatments go hand in hand and improve control over pain and improve the function and patient's quality of life while limiting drug toxicity.

Right now there is a lot of research being carried out for drug improvement for control of OA. But these drugs and procedures still need to be proven for clinical effectiveness and for long-term safety of patients. This proof is very important to avoid other problems, like gastro-intestinal problems, because OA mainly affects people of the age group of 60 who are more prone to drug toxicity. As a result, non-pharmacological treatments are preferred for such patients or those with co-morbidities. This is a very important area of research in OA since it will help to determine the severity of the disease and its progression and might eventually aim to halt or even revert the disease (Tanna, 2004).

Injection therapies have some rare complications, such as joint infection. Undue delay in treating such infections can lead to diminished joint movements and function. Fluid might ooze too fast. If the injected directly into tendons or nerves, it can cause severe damage. Color changes also may occur around injection sites in individuals with dark skin. Serious side effects more typically occur in people who are taking injections for long periods of time (MFMER, 1998-2006).

Physicians, therefore, limit the number of injections over a specific time period. Studies differ on exact recommendations on the limits due to the numerous variables involved. In general, the limit for osteoarthritic patients ranges from four injections per lifetime to one injection per month (MFMER, 1998-2006).

This is probably because there no defined procedure or a defined way for the therapy. Over the next decade, experimental therapies may be approved by the FDA. Until such time, oral medication and anti-inflammatory injection therapy along with physical therapy will continue to play a major role in managing pain in arthritic patients (MFMER, 1998-2006).

CHAPTER 7

CONCLUSIONS AND RECOMMENDATIONS

The present thesis modeled and analyzed the fluid flow in cartilages, both normal and damaged, found in synovial joints in the knee. The work considered various stages of damages, and different loading conditions that simulate the activity levels of the person. Normally encountered velocities for Walking and jogging were considered in analyzing the fluid flow. The results can be summarized as follows:

- For Case 1, the peak velocity for walking at this stage has a lower much value than that for running or jogging
- For case 2, the peak velocity for the latter activities, running and jogging, is lower than that in simple walking but the overall velocity is higher in the latter cases.
- For case 3, while the results were similar to Case 2, the velocities in case 3 of the last two activities (jogging and running) are higher than those in case two.
- For case 4, the difference is higher velocities of the fluid coming out of the cartilage. Performing activities like running take lesser time than walking.
- In the initial stages of the disease the velocity of the fluid is less than that in the later stages

This systematic approach to the flow of Synovial fluid and the parameters affecting the flow will help in better understanding the procedures adapted in the treatment. Addition of physiological variables that help in determining the right volume of fluid that can be injected depending on the onset of the decease is the main focus of this research which has not been reported the in the literature so far.

The following conclusions can be deduced from the current research.

- Physical attributes such as weight of the person and the onset of disease has can now be introduced as a variables that will determine the correct physical properties of the Synovial fluid that can be affectively used to treat patients.
- Next interval when the right volume of fluid can be injected has been effectively determined using the mathematical models.
- This research has shown its potential that would help prevent in administering medication irrespective of the variables discussed in the models and also prevents in administering excessive medication which would otherwise may lead to side effects in patients.

Future work:

The current models can be expanded to more detailed models that would include transient flow phenomenon in tissues during aggressive activities in patients. Possibly, a trail study may be conducted in willing subjects suffering from this decease under medical supervision to further evaluate the effect of mathematical parameters. Thus the models can be refined to become powerful device that help the medical services community in treating patients much more effectively and at reduced medical costs.

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