

Pelvic ring fractures: External fixation comparative numerical structural analysis

Original

Pelvic ring fractures: External fixation comparative numerical structural analysis / Ali, Shady; Giachino, Matteo; Bonani, Andrea; Aprato, Alessandro; Riyahi-Alam, S.; Khattab, Aly; Bignardi, Cristina; Massè, Alessandro. - ELETTRONICO. - (2015), pp. 10-14. (7th Cairo International Biomedical Engineering Conference, CIBEC 2014 Mena House Hotel, egypt 2014) [10.1109/CIBEC.2014.7020934].

Availability:

This version is available at: 11583/2731985 since: 2021-09-09T18:06:10Z

Publisher:

Institute of Electrical and Electronics Engineers Inc.

Published

DOI:10.1109/CIBEC.2014.7020934

Terms of use:

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

Publisher copyright

IEEE postprint/Author's Accepted Manuscript

©2015 IEEE. Personal use of this material is permitted. Permission from IEEE must be obtained for all other uses, in any current or future media, including reprinting/republishing this material for advertising or promotional purposes, creating new collecting works, for resale or lists, or reuse of any copyrighted component of this work in other works.

(Article begins on next page)

Pelvic Ring Fractures: External Fixation Comparative Numerical Structural Analysis

Shady Ali, Matteo Giachino, Andrea Bonani, Alessandro Aprato, S. Riyahi-Alam, Aly Khattab, Cristina Bignardi, and
Alessandro Massè.

Abstract— External fixation (EF) is commonly practiced for pelvic ring fractures management. Many parameters influence mechanical performances of external fixators. Our virtual 3D model of the pelvic ring introduces the advantage of differentiating the mechanical properties of cortical and cancellous bone along with the complex boundary conditions of major ligaments. We assessed stiffness variations by increasing fixator pins depth and we evaluated dislocation related to load intensity and sitting angle.

The 3D model was crafted from a real CT scan. Finite Elements Analysis was run on the model, reproducing a Tile's classification C1 fracture. A 600N load was applied with a 40, 50 and 60 mm pins depth configuration simulating sitting and standing conditions. Four typical body constitutions were probed for 15°, 30°, 45°, 60°, 75° and 90° sitting inclination. Dislocation was taken as stiffness index.

Rising pins depth to 60 mm reduces dislocation up to 22.8% in standing position and up to 15.5% in sitting simulation. Dislocation values tend to decrease along with sitting angle and initial weight.

On an external fixated pelvic ring, pins depth affects significantly the structure stiffness. Patient sitting angle and his initial weight has also great influence in dislocation.

Keywords— *Pelvic fractures; Finite elements analysis; External fixation; Mechanobiology.*

I. INTRODUCTION

Pelvic ring fractures represents about 2-3% of all fractures [1]; they are potentially life-threatening injuries due to the burden of complications frequently associated. Patients with this type of lesions are at high risk of fatal bleeding, transitory and permanent nerve injuries, infection and tromboembolism[2-4]. Prompt treatment choice has thus a crucial influence on patient's prognosis [5].

External fixation has gradually become a widely diffuse primary approach for this type of injuries; it is actually fast, relatively safe and a less invasive procedure compared to a definitive internal fixation [6-7].

Manuscript received in August 2014, accepted in October 2014.

Shady Ali (corresponding author), Mechanical Design and Production Engineering Department, Faculty of Engineering, Cairo University, Giza, Egypt. Also, Mechanical and Aerospace Engineering Department, Politecnico di Torino, Torino, Italy.

(E-mail: eng.shadysamir@hotmail.com).

Aly Khattab, Mechanical Design and Production Engineering Department, Faculty of Engineering, Cairo University, Giza, Egypt.

Matteo Giachino and Andrea Bonani are from School of Medicine, University of Turin, Torino, Italy.

Cristina Bignardi and S.Riyahi-Alam are from Mechanical and Aerospace Engineering Department, Politecnico di Torino, Torino, Italy.

Alessandro Massè and Alessandro Aprato are from Orthopaedic Department, School of Medicine, Orbassano, Italy

External fixation (EF) is commonly used for early fixation and can be also performed as definitive stabilization for rotational unstable type B fractures. For vertical unstable (type C) fractures EF represents a good temporary solution for the early management [8-9].

In the last decades several constructs of pelvic external fixators were introduced; all of them, with various design, were thought to obtain an acceptable stability for the injured pelvic ring. Archdeacon et al. have demonstrated that an orthogonal pelvic external fixator pin construct represents a better design in term of stiffness compared to a parallel pin construct [10]. Another characteristic that can affect stability of the pelvis-EF system is represented by pin diameter: Ponsen et al. have found that the use of greater diameter pins can improve stiffness until 20% [11]. Despite that, even the stiffest type of fixator has not yet guaranteed enough stability to allow patients early mobilization and weight bearing [11-12].

Driven by these considerations, we developed a reliable virtual 3D model of the pelvis, employing Finite Elements Method (FEM) to simulate the mechanical behavior of an EF-stabilized pelvic ring fracture. FEM analysis permits to divide a complex structure (e.g. the human pelvis with or without EF) in a high but finite number of simpler solids, allowing to calculate parameters like strains and stresses of the entire structure due to forces, displacements, structure load breaking points, and many others [20].

Other authors have already tried to analyze stresses sustained both physiologically and pathologically by the pelvis [12-19]; this is however the first study that muster up a more accurate pelvic design with the biomechanics of an unstable fracture, treated with an EF.

The first goal of the study was the implementation of a realistic virtual 3D model of the pelvis, considering properties of both cancellous and cortical bones, and the reproduction of the main stabilizing ligaments of the pelvic ring. The second target was to assess how pins depth affects the stability of the pelvis-EF system. The third one was the simulation of displacement rates of the injured pelvis with EF, related to different sitting angles (15°, 30°, 45°, 60°, 90°) in four different weight classes: a relevant issue involving a pelvic fractured patient is thus represented by his mobilization and nursing care.

II. METHODS

A 3D model of a complete human pelvis was simulated starting from computed tomographic (CT) scan data of a healthy female patient, performed for a non-orthopedic condition. CT images were acquired with 1mm slice interval and imported as DICOM image format into the three-

dimensional visualization software Mimics®10.0 (Materialize, Belgium)[21].

Density thresholds were used to delimitate volumes of the innominate bone and the sacrum; within the same bones a further discrimination between cortical bone and cancellous bone was performed.

The threshold for the cancellous bone was set from 226 to 564 HU (Hounsfield Units) and for the cortical bone was set from 565 to 1615 HU. Since different morphological structures do not have a unique HU value, completely automatic segmentation of complex images is generally impossible and, therefore, needs to be performed manually and interactively[20-22]. Contours for cortical and cancellous bone of the pelvis and the sacrum were obtained from the consequent segmentation. “Fig.1”

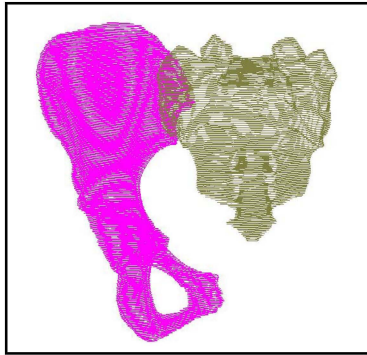


Fig 1.Contours of pelvis (cortical and spongy bone)

These contours were then imported to a Computer Aided Design (CAD) software (Rhino® 4.0, Robert McNeel & Associates, USA) to be transformed into a solid.

Components of the external fixator were designed with SolidWorks® software (Dassault Systèmes, France), the two hemi-pelvis and the sacrum were imported in the same software and assembled with the frame.

Fixator pins were placed one in the iliac crest, 1 cm posterior to the antero-superior iliac spine, and one supra-acetabular, in proximity of the antero-inferior iliac spine, as previously described[23]. “Fig.2”

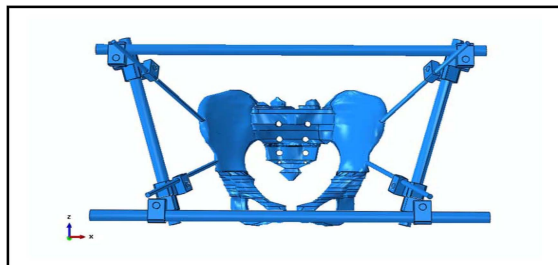


Fig 2.Complete CAD solid model

The model was imported into FEM analysis software Simulia Abaqus® 6.10-1 (Dassault Systèmes, France), to analyze the behavior of the fixator-pelvis system when loaded [20, 24]. Elastic modulus E [25] and Poisson ratio ν [26] of the different materials used are shown in table 1.

Table 1.Elastic Modulus (E) and Poisson ratio (ν) of the materials used in the model.

Materials	Elastic modulus E (MPa)	Poisson ratio (ν)
Cortical bone	16000	0.3
Cancellous bone	1600	0.3
Screws of external fixation (steel 316L)	190000	0.3
External fixation terminals (aluminum alloy)	72000	0.3
External fixation bars (composite material)	120000	0.3

The model presented linear elasticity and each component was a solid part. All components were meshed using C3D4: a 4-node linear tetrahedral element. In every model mesh sensitivity analysis was performed, providing 1498291 elements and 334978 nodes for the entire model.

Prior to analysis, boundary conditions were determined to define relations between parts. Sacrum was fixed and connected to one hemipelvis through an accurate representation of posterior stabilization complex ligaments (table 2).

Table 2. Parameters of main pelvic ring ligaments.

Ligaments	Stiffness (N/mm)	Number of springs
Sacroiliac	500	262
Sacrospinous	1500	6
Sacro-tuberous	1500	28
Iliolumbar	1000	25

The other hemi-pelvis was set free of connections, in order to simulate a Tile’s C1 fracture [27-28]. Cortical and cancellous bone were also tied together.

Different pin depths construct was the first parameter to be simulated. Depth of the screws was set at an increasing value of 40 mm, 50 mm and 60 mm both for superior and inferior access. The diameter of the screws was constantly set at 6 mm. Each model was then exposed to two loading conditions: respectively sitting and standing positions. Sitting simulation was performed by loading the pelvis on the ischiatic tuberosities (reaction of the sitting plane), standing position by loading the acetabula (reaction of femur head). No muscular loads have been considered. [10-12, 29-30]. For the standing position a 600N load, parallel to Z axis (90° from plane) was applied to the two acetabula. For the sitting position a 600N load, parallel to Z axis (90° from plane) was applied to the two ischiatic tuberosities. Load/displacement curve analysis was performed for every part of the pelvic ring and the external frame in order to check the stability of the system.

Next step was the stiffness variation evaluation related to load direction. To perform this analysis we only considered a 60 mm pins depth configuration, in light of previous analysis results.

Only in sitting position the load was inclined towards the XY plane with different angles: 90°, 75°, 60°, 45°, 30°, 15° in

clockwise direction. All loads have been applied concentrated on single nodes. Load/displacement curves analysis of the model at different angles was performed considering four different patient habitus: the 25th (61.1 kg) and 50th (71.3 kg) percentile of women body mass and the 50th (86.1 kg) and 75th (98.9 kg) percentile of men body mass [31]. "Fig.3"

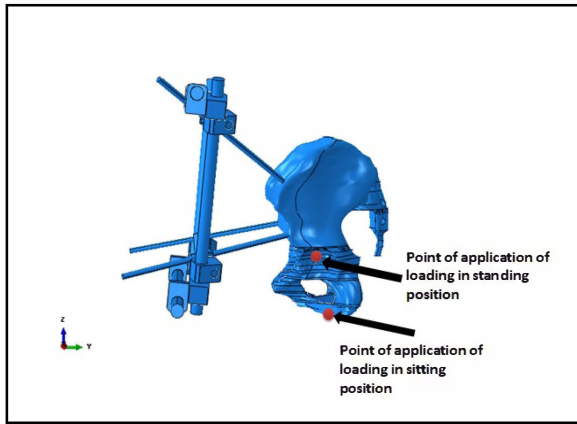


Fig 3. Loading condition at sitting position and standing position and the inclination of load about z axis.

According to biomechanical studies we set the maximum load on the pelvis as the total body weight without legs (about 60% of the total body weight [32]. If the trunk moves from a 90° position towards supine, part of the total load transfers to the back, lightening the pelvis bearing load. Vector resolution was performed to calculate the pelvic component of the total weight at each angle as shown in table 3. All loads values, in the different directions, results from the product of the body weight for 60%. Dislocation values at the sacroiliac joint and at the pubic symphysis were considered as main outputs.

Table 3. Loads applied to the ischiatic tuberosities in relation with wake up angle and mass percentile (N).

	90°	75°	60°	45°	30°	15°
25 th Women percentile	355	343	307	251	178	92
50 th Women percentile	414	400	359	293	207	107
50 th Men percentile	500	483	433	354	250	129
75 th Men percentile	575	555	498	407	288	149

III. RESULTS

Graphical representations of the results are depicted as a color code showing the displacement distribution (warm colors = higher displacements, cold colors = lower displacements) and its values in each model, according to the different loading conditions.

We analyzed stiffness related to pins depth for both standing and sitting position. Results are shown in table 4.

Table 4. Displacements observed related to pins depth (mm).

Pins depth	Sitting		Standing	
	Max displ.	S-I displ.	Max displ.	S-I displ.
40mm	26.47	18.13	32.08	18.34
50mm	24.34	16.91	26.9	16.95
60mm	22.59	15.7	24.75	15.6

Values for the sacroiliac joint (S-I) are the maximum displacements registered on articular bone interface. "Fig.4"

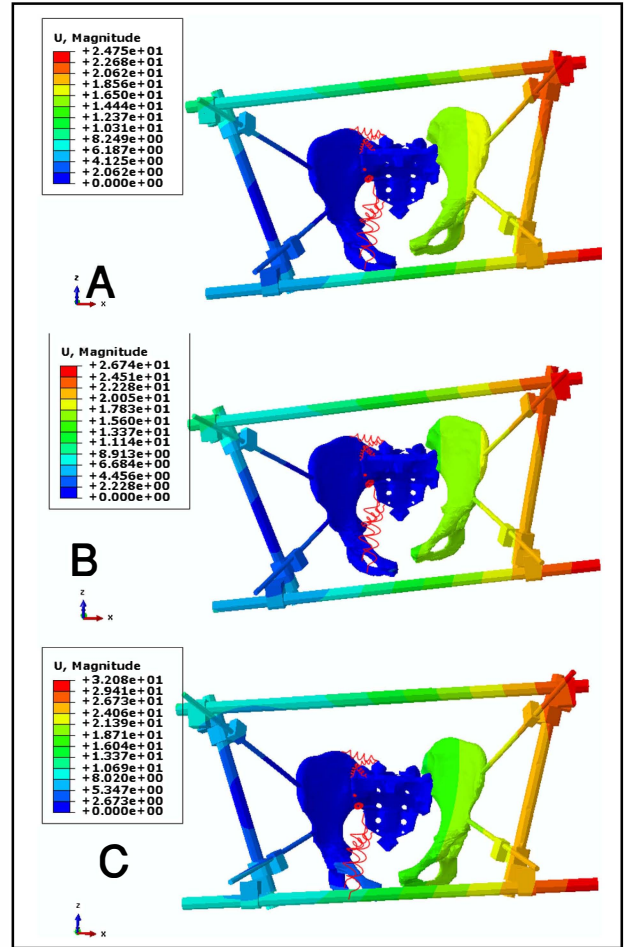


Fig 4. Displacement distribution for Pin Depth (A.60), (B.50), (C.40 mm) in standing position. Red wires represent ligaments.

The maximum displacement for standing position was reduced by 16.1 % and 22.8% rising pins depth respectively from 40 mm to 50 and 60 mm. Values obtained at the sacroiliac joint followed a similar trend. Maximum displacement for sitting position was reduced by 9 % and 15.5% rising pins depth respectively from 40 mm to 50 and 60 mm. At the sacroiliac joint the same reduction was observed. "Fig.5"

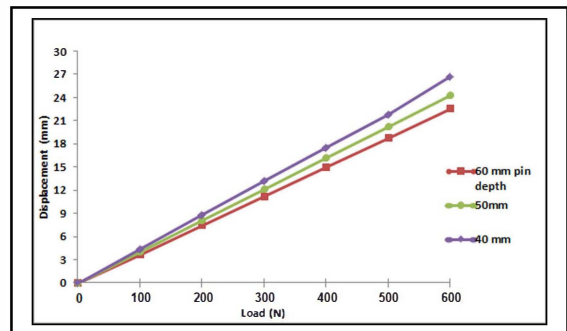


Fig 5. Displacement vs Load for Pin Depth (40, 50, 60) mm Of External Fixator Sitting Position.

Results for the simulations run at different sitting angles for the four body constitution categories are summarized in table 5 and 6.

Table 5. Sacroiliac displacement (mm).

	90°	75°	60°	45°	30°	15°
25thWomen percentile	9.23	8.58	7.06	5.02	3.74	2.12
50thWomen percentile	10.76	10	8.26	5.86	4.35	2.46
50th Men percentile	13	12.08	9.96	7.08	5.25	2.97
75th Men percentile	14.95	13.88	11.45	8.14	6.05	3.43

Table 6. Pubic symphysis displacement (mm).

	90°	75°	60°	45°	30°	15°
25thWomen percentile	8.52	10.29	8.29	6.02	3.92	2.02
50thWomen percentile	9.94	12	9.69	7.03	4.55	2.35
50th Men percentile	12	14.49	11.69	8.5	5.5	2.84
75th Men percentile	13.8	16.65	13.45	9.77	6.34	3.28

IV. DISCUSSION

External fixation of the pelvis is a commonly practiced procedure for both emergency and definitive treatment of unstable lesions. Although its decades of development, no frame configuration has by now nearly guaranteed a complete stability of the pelvis with physiological load [11-12], making an early patient mobilization unsuitable.

First main achievement of our work is the implementation of an accurate 3D virtual model of the pelvic ring that biomechanically considers ligaments and the difference between cortical and cancellous bone. No previous studies have put together all these information in a single model while simulating an injured pelvis. Comparisons with similar studies based on real models support the reliability of the data obtained [10-19]. Despite the high accuracy of our simulations, such a complex model would benefit from an experimental validation in future studies.

Pins depth is a major factor that affects stability of the fixator-pelvis system. Simulations run on our model showed a significant displacement reduction by plunging pins at 60 mm, compared to a 40 mm configuration. Stability is a key word of the traumatic pelvic pathology, a stiffness increase up to 22.8% and 15.5% respectively for standing and for sitting position with 60 mm screws is a worthy outcome that should be taken into consideration while pinning.

In our CT-based model, 60 mm was almost the maximum depth allowed by anatomy; this means it would be hard to reach such measure in every patient; however, as data show that the deeper the pins go the stiffer become the structure, it would be suitable to plunge pins as inward as possible.

For the first time we tried to focus on the relationships existing between patient's weight, sitting angles and load born by the pelvis. Sitting angle has, in fact, a crucial influence in pelvis load and its intensity. Whether at 90° the entire weight of trunk, upper limbs and head falls on the ischiatic tuberosities

intensely stressing the structure, at 45° approximately 70% of the total load charges the pelvis and this percentage reduces to 26% at 15°. This is independent of initial weight, suggesting that is suitable to allow a wider range of flexion in lighter patients. Our analysis takes into account sacroiliac and symphysis displacement, considering thus the biomechanical major segments of the pelvic ring [28, 33]. Posterior complex integrity has the absolutely main impact on stability and its reduction is of utmost importance for a good outcome [33]. By setting 5 mm as the maximum tolerable displacement for the maintenance of a satisfying reduction, we can cross-match the sitting angle theoretically permitted for each category of patients considered [34]. Our data show that the fixator-pelvis structure cannot bear a sitting angle above 45° in any case without causing an out-of-range displacement of anterior and posterior complex. At 45° only light patients (25th women percentile) maintain an acceptable reduction; an inclination of 30° is permitted for the 50th women percentile, while 50th men percentile slightly exceeds the limits of acceptance. Higher weights still suffer from excessive displacement. Only at 15° a less than 5 mm dislocation is granted for all the cases considered in the simulations.

Our simulations eventually suggest a much more conservative post-stabilization management of the injured patient. Clinical practice put a limit at 45° sitting angle for essentially all cases, being implicitly aware of the supplementary stress suffered from the structure in high weight people.

We simulated one of the most challenging condition for an external fixator, which is an entire hemi-pelvis without any connections to the controlateral. The whole load thus falls on the external construct. Literature suggests that soft tissues other than joint ligaments participate in pelvic ring biomechanics, smothering stresses of the bony part [29]; this consideration leads to believe that in reality we can expect a slightly better condition than what we found.

It is also important to consider that pelvic ring disruptions require long hospitalization and healing time; quality of life therefore represents a major goal during the treatment of this type of injuries. Even if the EF could not ensure a complete stability at high degrees of trunk flexion, a compromise between fracture healing and patient's quality of life (e.g. nutrition, nursing etc.) should be accepted.

EF has a widely popular indication for additional treatment of internal fixated pelvis fractures. A future application of our model will be the association of internal synthesis with an EF for the consequent analysis of the new biomechanical setting, which should be reasonably much stiffer than the EF alone. A further analysis will be the simulation of a horizontally unstable Tile's B fracture, where EF alone sometimes represents a reasonable treatment choice.

As a conclusion, an accurate virtual 3D model of the human pelvis has been implemented, considering bone and ligaments biomechanics. The analysis of pelvis model with external fixator proved that pins depth affects stiffness of the externally fixated pelvis. A 60 mm deep configuration reduces respectively by 22, 8% and 15, 5% the dislocation of the unbound hemi-pelvis in standing and sitting position. In light

of previous results and considerations we also believe that a tailored indication based on patient's weight for post-stabilization management will be suitable for maximizing healing outcome.

ACKNOWLEDGMENTS

The authors declare that no professional or financial affiliations have biased the presentation.

REFERENCES

- [1] Balogh, Zsolt, et al. "The epidemiology of pelvic ring fractures: a population-based study." *Journal of Trauma-Injury, Infection, and Critical Care* 63.5 (2007): 1066-1073.
- [2] Wong, James Min-Leong, and Andrew Bucknill. "Fractures of the pelvic ring." *Injury* (2013).
- [3] Hauschild, Oliver, et al. "Mortality in patients with pelvic fractures: results from the German pelvic injury register." *Journal of Trauma-Injury, Infection, and Critical Care* 64.2 (2008): 449-455.
- [4] Kido, Akira, Fumitaka Inoue, Yoshinori Takakura, and Toru Hoshida. "Statistical analysis of fatal bleeding pelvic fracture patients with severe associated injuries." *Journal of orthopaedic science* 13, no. 1 (2008): 21-24.
- [5] Verbeek, Diederik, et al. "Acute management of hemodynamically unstable pelvic trauma patients: time for a change? Multicenter review of recent practice." *World journal of surgery* 32.8 (2008): 1874-1882.
- [6] Stahel, Philip F., et al. "External fixation for acute pelvic ring injuries: Decision making and technical options." *Journal of Trauma and Acute Care Surgery* 75.5 (2013): 882-887.
- [7] Rubel, Iván F., Peter Kloen, Olivier Borens, and David L. Helfet. "External fixation for pelvic ring injuries." *Techniques in orthopaedics* 17, no. 2 (2002): 221-227.
- [8] Bircher, M. D. "Indications and techniques of external fixation of the injured pelvis." *Injury* 27 (1995): B3-19.
- [9] Riemer, Barry L., et al. "Acute mortality associated with injuries to the pelvic ring: the role of early patient mobilization and external fixation." *Journal of Trauma and Acute Care Surgery* 35.5 (1993): 671-677.
- [10] Archdeacon, Michael T., et al. "Orthogonal pin construct versus parallel uniplanar pin constructs for pelvic external fixation: a biomechanical assessment of stiffness and strength." *Journal of orthopaedic trauma* 23.2 (2009): 100-105.
- [11] Ponsen, Kees-jan, Pieter Joosse, Gilbert A. Hoek Van Dijke, and Chris J. Snijders. "External fixation of the pelvic ring: an experimental study on the role of pin diameter, pin position, and parasymphyseal fixator pins." *Acta orthopaedica* 78, no. 5 (2007): 648-653.
- [12] Ponsen, Kees J., Gilbert A. Hoek van Dijke, Pieter Joosse, and Chris J. Snijders. "External fixators for pelvic fractures: comparison of the stiffness of current systems." *Acta Orthopaedica* 74, no. 2 (2003): 165-171.
- [13] Anderson, Andrew E., Christopher L. Peters, Benjamin D. Tuttle, and Jeffrey A. Weiss. "Subject-specific finite element model of the pelvis: development, validation and sensitivity studies." *Journal of biomechanical engineering* 127, no. 3 (2005): 364-373.
- [14] Dalstra, Michel, R. Huiskes, and L. Van Erning. "Development and validation of a three-dimensional finite element model of the pelvic bone." *Journal of biomechanical engineering* 117, no. 3 (1995): 272-278.
- [15] Dalstra, Michel, and R. Huiskes. "Load transfer across the pelvic bone." *Journal of biomechanics* 28, no. 6 (1995): 715-724.
- [16] Garcia, J. M., et al. "Three-dimensional finite element analysis of several internal and external pelvis fixations." *Journal of biomechanical engineering* 122.5 (2000): 516-522.
- [17] Goel, V. K., S. Valliappan, and N. L. Svensson. "Stresses in the normal pelvis." *Computers in biology and medicine* 8, no. 2 (1978): 91-104.
- [18] Oonishi, Hironobu, Hideo Isha, and Tatsuhiko Hasegawa. "Mechanical analysis of the human pelvis and its application to the artificial hip joint—by means of the three dimensional finite element method." *Journal of biomechanics* 16, no. 6 (1983): 427-444.
- [19] Thompson, M. S., M. D. Northmore-Ball, and K. E. Tanner. "Effects of acetabular resurfacing component material and fixation on the strain distribution in the pelvis." *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine* 216, no. 4 (2002): 237-245.
- [20] Andreaus, Ugo, and Daniela Iacoviello. *Biomedical Imaging and Computational Modeling in Biomechanics*. Springer, 2013.
- [21] Dabrowska-Tkaczyk, Anna, and Marek Pawlikowski. "Influence of remodelling, stimulating factor selection on bone density distribution in pelvic bone model." *Acta of Bioengineering and Biomechanics* 8, no. 2 (2006): 119.
- [22] Boissonnat, Jean-Daniel. "Shape reconstruction from planar cross sections." *Computer vision, graphics, and image processing* 44, no. 1 (1988): 1-29.
- [23] Uslenghi M, Alluto C, Governale G, et al. "La fissazione esterna di bacino: studio morfometrico della pelvi." *Minerva Ortopedica e Traumatologica*. 60.4 (2009):255-260.
- [24] Kluess D, Wieding J, Souffrant R, Mittelmeier W, and Bader R. "Finite Element Analysis in Orthopaedic Biomechanics" In: *Finite Element Analysis, Sciyo, Rijeka, Croatia*. Hrsg: David Mortal. (2010): 151-170.
- [25] Askeland DR, Phulé PP. *The science and engineering of materials*. (5th ed.). Cengage Learning 2006; 198.
- [26] Boresi, Arthur Peter, Richard Joseph Schmidt, and Omar M. Sidebottom. *Advanced mechanics of materials*. Vol. 6. New York: Wiley, 2003.
- [27] Pennal, George F., Marvin Tile, James P. Waddell, and Henry Garside. "pelvic disruption: assessment and classification." *clinical orthopaedics and related research* 151 (1980): 12-21.
- [28] Tile, Marvin. "Acute pelvic fractures: I. Causation and classification." *Journal of the American Academy of Orthopaedic Surgeons* 4, no. 3 (1996): 143-151.
- [29] Phillips, A. T. M., P. Pankaj, C. R. Howie, A. S. Usmani, and A. H. R. W. Simpson. "Finite element modelling of the pelvis: inclusion of muscular and ligamentous boundary conditions." *Medical engineering & physics* 29, no. 7 (2007): 739-748.
- [30] Bergmann, G., et al. "Hip contact forces and gait patterns from routine activities." *Journal of biomechanics* 34.7 (2001): 859-871.
- [31] Fryar CD, Gu Q, Ogden CL. *Anthropometric reference data for children and adults: US population, 2007-2010*. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics, 2012.
- [32] de Leva P. "Adjustments to Zatsiorsky-Seluyanov's segment inertia parameters." *J Biomech*. 29.9 (1996):1223-1230.
- [33] Tile, Marvin, David Helfet, and James Kellam, eds. *Fractures of the pelvis and acetabulum*. Vol 2 . Lippincott Williams & Wilkins, 1995.
- [34] Matta, Joel M. "Operative treatment of acetabular fractures through the ilioinguinal approach A 10-year perspective." *Clinical orthopaedics and related research* 305 (1994): 10-19.