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In vitro biomechanical testing of the stability of primary and revision hip acetabular implants

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Abstract

Aseptic loosening of the hip acetabular component is the main cause of failure of hip arthroplasty and is the consequence of lack of implant stability in the early post-operative period.

Hip acetabular stability is the capability of acetabular implants to resist to the forces acting in the acetabulum during patient activities after surgery. If implant motions are sufficiently low, primary stability is achieved and the osteointegration process between the implant and the surrounding bone may occur. In this context, measuring implant motions is essential to predict the implant failure. In clinical practise this is achieved by the analysis of radiographical images acquired in consecutive patient follow-ups. These measurements are limited to the implant migration, while elastic motions and periacetabular strains, that contribute to implant stability, are not monitored. So far, to obtain a complete set of stability measurements with high accuracy, *in vitro* testing is the most reliable option. Despite the importance of the experimental analysis, a general consensus about the application of biomechanical tools to solve clinical problems is still missing.

The aim of my Ph.D project was to develop and apply reliable *in vitro* methods to assess the hip acetabular stability in case of primary and revision reconstructions.

First, two methodological studies were conducted (1) to define and implement a robust reference frame for the human hemipelvis based on a morphological analysis of this anatomical district and (2) to create a robust procedure to measure the implant motions and the periacetabular strains with the Digital Image Correlation technique. Secondly, I applied these methods to answer the following clinical questions:

1. How do changes in the motor task affect the cup stability and the periacetabular strains?

   Both walking and standing up motor tasks generated implant migration comparable with the clinical observations. The cranial translation of the cup was the highest motion component measured during walking, while standing up generated the highest rotations of the implant. The largest periacetabular strains where measured during standing up. Such results suggested that preclinical testing of new uncemented press-fit cups should include the simulation of both the motor tasks. Moreover, the

study could also translate to indication of which motor activity should be avoided in critical clinical cases.

2. Does the cup medialization affect implant stability?

   The resultant cup migration was slightly larger when the cup was medialized if compared with an anatomical reconstruction. The rotations had a similar trend. In almost all the cases, the cup motions faced by the implant in the two implantation configurations were not statistically different. The results suggested that cup medialization does not improve initial cup stability and, considering the influence of medialization on hip biomechanics, conventional reaming should not be routinely performed.

3. Which is the effect on cup stability of defect reconstructions with an innovative synthetic bone substitute or with human bone graft in revision surgery?

   The two reconstruction materials provided similar mechanical stability in terms of permanent and inducible motions at reasonable load levels for post-op patients (up to 3 BW). The results suggested that the synthetic graft presented in the study could be used as a reliable alternative solution for acetabular defect filling in revision cases of severe, contained defects overcoming the issues of human bone graft in terms of availability, costs and body-rejection.

To conclude, this project provided a new reliable collection on *in vitro* methods to perform biomechanical testing on human hemipelvis specimens and to assess the stability of acetabular reconstructions by mean of Digital Image Correlation. As the use of this measurement technique is spreading in the biomechanical field, my project may constitute the starting point for future investigations on cup implant stability. Moreover, due to the versatility of the Digital Image Correlation, my methods could be also applied to assess the stability of different prosthetic devices adopted for the acetabular reconstructions.

Content

Chapter 1: Introduction

1.1 Overview of anatomy and biomechanics of the hip

The hip is the anatomic structure of the human body connecting the axial skeleton to the lower extremities. Its function is to carry the upper body weight and transfer forces from the ground up: this must be accomplished allowing the maintenance of equilibrium and balance while standing and during the motor activities. This complex functional role is reflected in the anatomical complexity of the hip (Fig. 1.1).

Biologically, the hip joint is classified as synovial joint: it is a cavity internally covered with articular cartilage, surrounded by a ligamentous capsule and capable to produce synovial fluid[1]. It is formed by the head of the femur and the acetabulum of the pelvis constituting a ball-and-socket joint, thus having 3 rotational degrees of freedom while translations, in case of healthy hip, are negligible[2]. This is allowed by the congruency of the articulating surfaces.

The hip stability is provided by a series of anatomical structures. A contribution is exerted by the *labrum*, a fibro-cartilaginous strip attached to the acetabular rim that helps in the dissipation of the forces across the hip and in avoiding excessive hip motions by improving joint congruity.

The ligamentous capsule contributes significantly to hip stability. It is formed by 3 ligamentous sheets arising from the periphery of the acetabulum and extending down to the femoral neck, twisting around the hip joint. They oppose to the joint distraction. Inside the joint, the *ligamentum teres*, connecting the femoral head with the acetabular fossa, stabilizes the hip during external rotations.

The major contribution is provided by the 22 muscles acting on the hip joint, supplying stability and exercising the forces required for the hip motion. Among them, the hip abductors play the major role in stabilizing the pelvis during single leg stance, as a compensation of the moment generating by the body weight[3].

The study of the hip biomechanics is fundamental for understanding the effect of alterations in the hip anatomy on joint stability and for planning surgical replacement. Osteoarthritis, the progressive debridement of the articular surfaces causing pain, in

example, can be reduced by reducing the joint reaction force: this may be achieved by reducing the body weight, the lever arm of the body weight or by introducing a compensation at the opposite side of the painful hip (such as the use of a walking stick) so as to reduce the hip abductor force acting on the painful hip[4,5].

However, in case of excessive degeneration of the hip biomechanical function, generally associated with pain, the treatment is represented by the surgical hip replacement also known as hip arthroplasty.

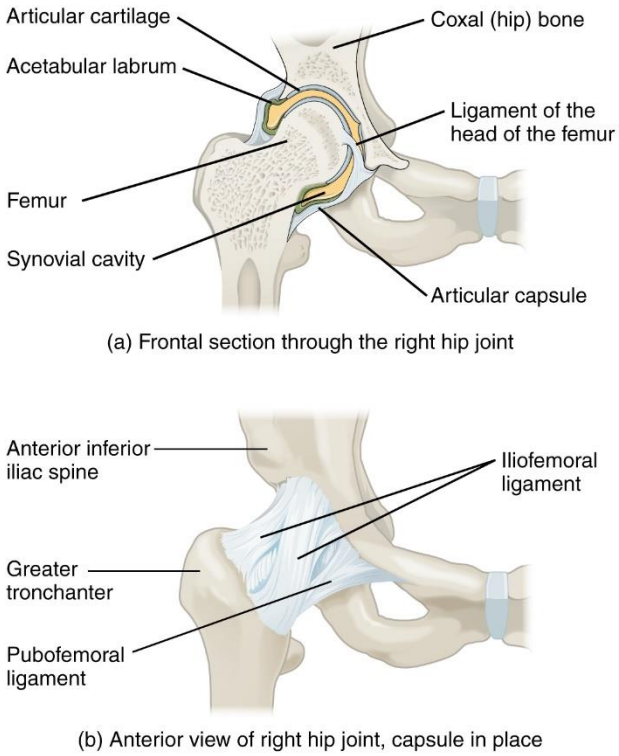

Fig. 1.1: The main anatomical structures of the hip bone

1.2 Hip arthroplasty

Hip arthroplasty is the surgical replacement of the hip joint with artificial mechanical components, aiming the restoration of the hip joint function (Fig. 1.2). In most cases, the replacement involves both the acetabulum and the femur, but it may be also partial (hemiarthroplasty).

The main cause of primary hip replacement is osteoarthritis accounting for more than 70% of the cases. Implant fixation is related to the patient age: press-fit uncemented cup are mainly adopted in younger patient, due to the higher physical demand and the presence of reactive bone; for elder patient the cemented fixation is usually preferred[6,7,8,9,10]. An exception to this trend is represented by hip arthroplasty performed in the USA where uncemented fixation is adopted in almost all cases[11]. Overall, the use of cemented fixation is progressively decreasing also for elder patients.

About 10% of primary implants fail, requiring a new surgical replacement for the patient and aseptic loosening of the acetabular component is the most frequent cause of failure.

Aseptic loosening is a multi-factorial event caused by the presence of debris around the acetabular cup that progressively leads to the formation of fibrous tissue at the bone/prosthesis interface[12,13]. Such debris can have multiple origins but are always related to a lack of acetabular primary stability.

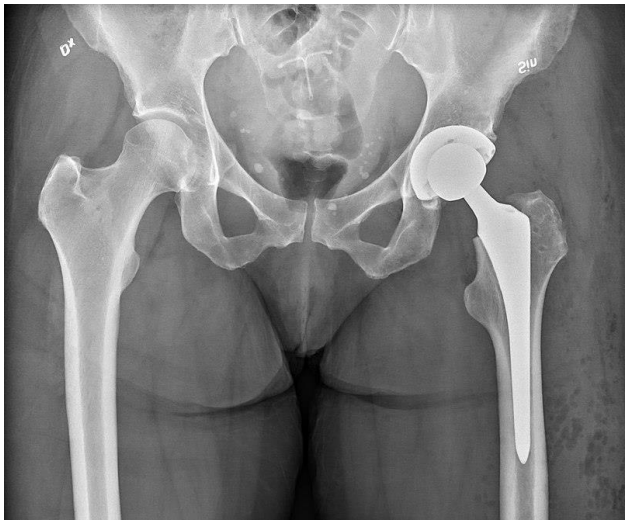

Fig. 1.2: Hip arthroplasty. The picture shows a left hip reconstruction

1.3 Hip acetabular stability

Implant stability is a measure of the clinical immobility of an implant. When an acetabular cup is press-fitted in the hip cavity, it engages peripherally with the cortical bone. Therefore, primary stability is mainly provided by mechanical factors, i.e. the interference friction, the microscopic interlock between cup and bone and occasionally macroscopic features such as fins, threads, pegs and screws[14]. Other factors influencing primary stability are the bone quality and the surgical technique. The achievement of primary stability is a requirement for secondary stability namely osteointegration (biological stability). Osteointegration is the fusion of the implant with the underlying bone, occurring 3-4 weeks after the implantation and is activated by the lesion of the pre-existing bone matrix during cup insertion. The exposure of the matrix to extra-cellular fluid stimulates bone regeneration and remodelling. Factors influencing osteointegration are the implant biocompatibility, the implant surface roughness and porosity and the cup motions[15]. It has been demonstrated that if excessive micromotions occur during the first stages of osteointegration, fibrous tissue arises in the interface between cup and bone, compromising secondary stability. *In vivo* studies performed on animal models showed that micromovements greater than 150 μm lead the formation of fibrous tissue; micromovements lower than 40 μm allow osteointegration; micromovements between 40 and 150 μm lead to a variable outcome[16,17,18]. For the sake of clarity, it is important to distinguish among two typologies of implant motions: the cup migration and the cup elastic motions. Even if the cup is forced in the acetabular cavity in press-fit implantation, it is expected that the implant will settle during the first load applications (e.g. during rehabilitation) so as to reach a stable permanent configuration. If this migration is limited, with no impacts on the anatomy and on the biomechanics of the reconstructed hip joint, it will not compromise secondary stability. Conversely, an excessive cup migration is correlated to the risk of late aseptic loosening of the implant. For this reason, many authors identified clinical thresholds for the cup migration, measurable in clinical practise, to use as predictors for cup mobilization[19].

The elastic cup motions arise during the load application and are recovered when the acetabulum is unloaded. As they generate during hip motion, they cannot be assessed

clinically through the analysis of radiographic images, but still compromise cup stability if excessive. For this reason, monitoring the elastic motions is of outstanding importance. Beside implant motions, strains may play a role in hip implant stability. The implantation alters the load transfer from the cup to the pelvic bone during motor activities, leading to a re-distribution of the anatomical structures surrounding the implant. This biological mechanism was thoroughly investigated and is well known as Wolff's law[20]: the living bone undergoes a local adaptation of the internal trabecular architecture and of the external cortical shell in relation to the local force stimulus. As a result, the bone becomes thicker and denser in regions withstanding high loads and weaker and less dense where the force stimulus is reduced: such phenomenon is also known as stress-shielding effect.

1.4 *In vitro* assessment of cup stability: State of the art

Monitoring the magnitude of the cup motions is necessary to predict the late implant failure. *In vivo* measurements would be the most reliable quantities to achieve this goal, but due to ethical considerations, studies on living subjects are currently limited to animal models[21,16]. The clinical evaluation of cup stability provides the surgeons the status of the implant migration through the analysis of bio-images (usually radiographs) of the patient in a static condition; therefore, elastic motions and/or strains in the hip are not monitored. Such limitations may be overcome by the *in vitro* studies. *In vitro* studies represent a trade-off between the use of reliable simplified testing and the measurable clinical parameters. Moreover, they are required before clinical trials. In orthopaedics, clinical trials are performed to certificate the efficiency of biomedical devices, by investigating their interaction with the living human body in selected patients. As clinical trials are extremely tightened by ethical motivations and high costs, they can be performed only if such devices passed positively a series of pre-clinical tests such as *in vitro* functional testing.

However, despite the importance of *in vitro* experimentation, a general consensus on how to perform biomechanical testing is still missing.

The aim of this chapter is to provide a general overview of the current status of the art of experimental analysis of cup stability.

1.4.1 Inclusion criteria for the review

The selection process of the studies to include in the review is presented in Fig. 1.3

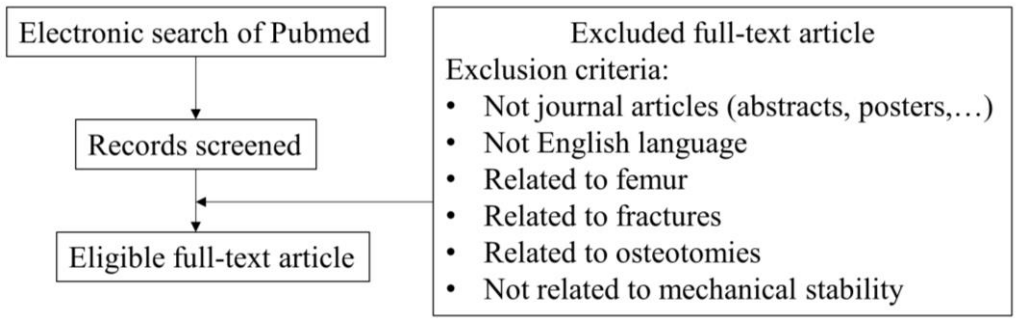

Fig. 1.3: Research strategy adopted in the present literature review

The source Pubmed was interrogated on March 2019. Three logical researches were adopted:

1. ((experimental) **OR** (in vitro) **OR** (biomechanics) **OR** (biomechanical)) **AND** ((acetabulum) **OR** (acetabular) **OR** (cup)) **AND** (stability)
    - N=420 studies were identified
    - **N=42** studies were eventually selected after the application of the exclusion criteria
2. ((experimental) **OR** (in vitro) **OR** (biomechanics) **OR** (biomechanical)) **AND** ((acetabulum) **OR** (acetabular)) **AND** ((defect) **OR** (defects))
    - N=209 studies were identified
    - N=15 were selected after the application of the exclusion criteria
    - **N=2** studies were eventually selected after the removal of the studies already selected
3. ((experimental) **OR** (in vitro) **OR** (biomechanics) **OR** (biomechanical)) **AND** ((acetabulum) **OR** (acetabular)) **AND** (revision)
    - N=263 studies were identified
    - **N=0** studies were eventually selected after the removal of the studies already selected

In addition, the bibliography of each selected paper was analysed, but no additional studies were reviewed.

Therefore, **N=44** studies were eventually reviewed (Tab. 1).

Tab. 1: List of papers included in the review

Author	Bone model	Implantation	Test	Measurements
Arts *et al.*[22]	Composite cylinder	Press	Torsion	Optical
			Lever-out	
Adler *et al.*[23]	Block of PU foam	Manual	Torsion	Test machine
	Bovine	Press	Lever-out	
Amirouche *et al.*[24]	Cadaveric hemipelvis	Manual	Monotonic ramp	LVDT
Baleani *et al.*[25]	Block of PU foam	Press	Torsion	Test machine
Beckmann *et al.*[26]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Optical
Beckmann *et al.*[27]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Optical
Beckmann *et al.*[28]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Optical
Bolder *et al.*[29]	Composite cylinder	Press	Torsion	Optical
Burkner *et al.*[30]	Block of PU foam	Press	Monotonic ramp	LVDT
Clarke *et al.*[31]	Cadaveric hemipelvis	Manual	Torsion	Test machine
Crosnier *et al.*[32]	Block of PU foam	Press	Cyclic physiologic	LVDT
			Push-out	Test machine
Crosnier *et al.*[33]	Block of PU foam	Press	Cyclic physiologic	LVDT
Curtis *et al.*[34]	Cadaveric hemipelvis	Manual	Torsion	Test machine
Fehring *et al.*[35]	Cadaveric hemipelvis	Manual	Manual bending	LVDT
Goriainov *et al.*[36]	Composite cylinder	Press	Torsion	Test machine
Hsu *et al.*[37]	Block of PU foam	Press	Lever-out	Laser
Huber *et al.*[38]	Composite acetabulum	Press	Lever-out	LVDT
Jacofsky *et al.*[39]	Cadaveric hemipelvis	Manual	Monotonic ramp	Optical
			Cyclic physiologic	
Jahnke *et al.*[40]	Block of PU foam	Drop weight	Torsion	Eddy current
Kanda *et al.*[41]	Block of PU foam	Press	Torsion	Torsiometer
				Dynamometer
Kwong *et al.*[42]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Extensometer

Lachiewicz *et al.*[43]	Cadaveric hemipelvis	Manual	Monotonic ramp Torsion	Strain gauge
Le Cann *et al.*[44]	Block of PU foam Bovine	Press	Lever-out Pull-out	Test machine
Macdonald *et al.*[45]	Block of PU foam Composite cylinder Cadaveric hemipelvis	Manual	Pull-out Lever-out Torsion	Test machine
Markel *et al.*[46]	Block of PU foam	Press	Lever-out	Laser
Meneghini *et al.*[47]	Composite hemipelvis	Manual	Lever-out	Test machine
Meneghini *et al.*[48]	Composite hemipelvis	Manual	Lever-out	Test machine
Michel *et al.*[49]	Bovine	Drop weight	Lever-out	Dynamometer
Michel *et al.*[50]	Cadaveric hemipelvis	Manual	Lever-out	Dynamometer
Milne *et al.*[51]	Block of PU foam	Press	Lever-out Torsion Push-out	Test machine
Olory *et al.*[52]	Block of PU foam	Manual	Lever-out	Manual
Perona *et al.*[53]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Eddy current
Pitto *et al.*[54]	Pelvis in PU foam	Manual	Cyclic physiologic	Eddy current
Plominski *et al.*[55]	Block of resin	Manual	Cyclic physiologic Lever-out	Test machine
Ries *et al.*[56]	Pelvis in PU foam	Press	Lever-out Pull-out	Test machine
Schwarz *et al.*[57]	Block of PVC foam	Manual	Lever-out	Test machine
Small *et al.*[58]	Block of PU foam	Press	Lever-out	Test machine
Stiehl *et al.*[59]	Cadaveric hemipelvis	Manual	Cyclic physiologic	LVDT
Tabata *et al.*[60]	Block of PU foam	Press	Torsion	Test machine
von Schulze *et al.*[61]	Cadaveric acetabulum	Manual Press	Lever-out	Test machine

Walschot *et al.*[62]	Composite cylinder	Press	Cyclic physiologic	Optical
			Lever-out	Test machine
Weiβmann *et al.*[63]	Block of PU foam	Press	Pull-out	Test machine
			Lever-out	
Widmer *et al.*[64]	Cadaveric hemipelvis	Manual	Monotonic ramp	Test machine
Wu *et al.*[65]	Cadaveric hemipelvis	Manual	Cyclic physiologic	Laser
				Strain gauge

1.4.2 Issues related to the bone model

The bone model has an influence on the final output of the study. Simple model, such as blocks of polyurethane (PU), allow to obtain repeatable results due the low inter-specimen variability. Models with an accurate anatomy, such as cadaveric models, are less repeatable but allow to obtain results closer to the real outcomes. For this reason, the choice of the bone model should be made in relation to the aim of the study.

Simple synthetic models

Several studies adopt PU models, in shapes of regular blocks, with controlled density[23,25,30,32,33,37,40,41,44,45,46,51,52,58,60,63]. This material aims to simulate the trabecular bone, with a density consistent with the density of the acetabular cancellous bone.

These models are available in the market, extremely cheap and the controlled manufacturing guarantees a low inter-specimen variability. On the other hand, the stiffness, frictional and yield behavior are significantly different from those of acetabular bone, limiting considerably their reliability in the assessment of primary stability, which, conversely, relies on the capability of the cup to grip the bone cortical outer rim of the acetabulum. To overcome this limitation and better mimic the mechanical properties of the acetabulum, in some studies synthetic models constituted by tubes of glass-fiber reinforced epoxy resin were adopted[22,29,36,45,62]. The tubes were machined to create the proper cavity for cup insertion. Therefore, primary stability was provided by the mechanical engagement of the implant with the rigid outer rim of the tube.

Animal bone specimens

An alternative to synthetic models is represented by animal bone specimens, which should present mechanical properties (yield, friction, damage criterion) more similar to those of human bone. As the anatomy of the animal bone, usually constituted by a quadruped hip, differs remarkably from the anatomy of the human bone, these models require to be adapted before the cup implantation. To the Author's knowledge in only one case the animal model, constituted by a primate pelvis, was kept intact for the experimentation[66]. In other studies, the bovine humerus and the bovine femoral epiphysis were used. The bones were cut in shape of blocks and sunk in resin blocks to allow preparation, implantation and test[23,44,49].

Despite animal models represent an improvement from synthetic models in mimicking the mechanical properties of human bone, significant limitations still persist, due to the different anatomical structure, deriving from the adaptations of the bone to withstand a quadrupedal deambulation.

In general, simple models are reliable in comparative studies, in which the question is not strictly related to the load distribution. However, if the aim of the study is related to the mechanical behaviour of the bone, simple models are not sufficiently representative, and anatomical models may provide richer information.

Anatomical models

Anatomical pelvis model made of composite material are frequently adopted in *in vitro* studies[27, ,47,48,67,68]. They are formed by a shell of glass-fiber reinforced epoxy resin with an infill of PU foam, aiming to mimic the double-layered structure of the human bone. Some studies reported values of overall stiffness 2 times larger than the stiffness measured in the human cadaveric pelvis. Also, strains measured around the acetabulum and in the iliac wing of composite specimens were larger than strains measured in cadaveric specimen, with a different orientation for the principal strains[69]. Like for PU models, the main advantages in using composite models are the cost (if compared with human models) and the low inter-specimen variability, allowing reproducible biomechanical testing.

So far, the use of cadaveric specimens for orthopaedic biomechanics research is the most accurate option in terms of morphology and anatomical structures. This allows the specimen preparation and implantation to be qualitatively and quantitively close to those performed in the clinical practise. In addition, human models represent the most reliable specimens for *in vitro* testing in terms of mechanical properties that are comparable with those of the living bone both in case of fresh-frozen specimens or embalmed[70]. For this reason, they are adopted in several studies[24,28,26,31,34,35,39,42,43,53,59,61,64,65]. Beside ethical constraints, the use of cadaveric specimens is limited by the cost, the availability and the difficulties in handling and preservation. Due to the fast specimen deterioration, *in vitro* testing are temporally limited (e.g no fatigue test can be conducted) and in any case the specimens must be kept wet during the testing. Moreover, cadaveric specimens may have a wide inter-specimen variability[71].

1.4.3 Issues related to the implantation technique

The implantation of the acetabular component is fundamental to have a good stability. Surgeons use *ad hoc* tools that are generally formed by a rod (impactor) which can be threaded to the cup at one extremity while the opposite side is flat and is hammered by the surgeon to settle the cup in the acetabular socket, previously reamed. The stability is manually assessed by slightly toggling the impactor. The force necessary to properly press-fit the cups was measured with instrumented surgical hammers and covers a range of 1.5 kN -9 kN[50,72,73] but may vary depending on the bone quality of the patient (e.g in case of osteoporosis).

Simplified approach

A simple model for cup implantation in *in vitro* applications consists in applying a constant load trough a press machine[22,25,29,30,32,33,36,38,41,44,46,56,58,60, 62,63]. The compression force varies in relation to the bone model adopted in the study generally constituted by blocks of synthetic bone[25,30,32,33,41,44,46,58,60,63]. This approach provides a low inter-specimen variability, but the final outcome (complete congruency) is not well representative of the clinical outcome (i.e. the polar gap between the implant and the acetabular wall is not achieved). Moreover, this procedure may be not applicable in

anatomical bone models, where impacts with high energies are required to grant cup insertion.

The application of quasi-static loads for the implantation is far from what is performed in clinical practise. To simulate the sequence of impacts that surgeons apply clinically, in a controlled way, some authors adopted a drop-weight approach[49,74,75]. This approach consists in make a mass, with a controlled weight, fall from a fixed height to hit the flat base of the surgical impactor, placed vertically on the acetabular socket. First, the mass is aligned with the impactor by a horizontal sliding and then is released. The vertical sliding allowed to set the proper height to generate the force necessary to press-fit the cup (usually larger than 2 kN). The number of impacts to properly settle the implant is generally assessed experimentally[40,49,75].

Realistic approach

A common and more realistic approach consist in implanting the device manually, as it is done operatively during hip replacement[23,24,26,27,28,31,34,35,39,42,43,45,47,48,50,52,53,54,55,57,58,61,64,65,]. The implantation is usually performed by a surgeon following the manufacturer's guidelines. The force required for implant insertion is based on the surgeon experience and the quality of the fixation is manually assessed. This approach is mainly adopted on anatomical specimens and it is more affected by inter/intra-operator variability[76].

1.4.4 Issues related to the load

Simple tests

In simple models the cup is forced to migrate in a direction imposed by the operator. Bone models in shape of regular blocks are usually adopted and are aligned so as to have the acetabular plane perpendicular with the axis of the testing machine or aligned with it, depending on the type of mechanical test. The same approach is used in case of biological models (animal or cadaveric) completely sunk in bone cement in which only the acetabulum is exhibited.

Pull-out and push-out tests allow to evaluate the out-of-plane migration of the cup, in a direction that is perpendicular to the acetabular plane. In case of pull-out tests, a rod is firmly fixed to the cup while the specimen is constrained to the mechanical setup. A traction load is then applied and the load necessary to distract the cup is measured [44,45,56,63]. Push-out tests consist in applying a vertical compression at the dome of the cup, through a hole at the base of the acetabulum. The hole should not influence the stress/strain distribution over the specimen due to its negligible mechanical effect during load in the intact pelvis[32,51]. Like for the pull-out test, the load necessary to distract the cup is measured. As the direction of load (as well as the direction of the cup migration) is not physiological, such tests are usually used to compare the frictional properties of cups implanted in bone surrogates.

Torsion tests allow to measure micromotions in the plane of the acetabular cup. The load is generally transmitted through a rod rigidly connected to the acetabular cup at one side and vised at the testing machine at the opposite side. The applied load is generally a combination of torsion and compression[22,23,25,29,31,34,36,40,41,43,45,51,60]. The displacement/load required to distract the cup is recorded through the testing machine. Torsion tests allow to assess the effects of the bearing frictional torques on hip stability, with cups implanted in synthetic bon models.

Lever-out tests allow to measure micromotions out of the plane of the acetabular cup, better simulating a failure scenario with respect of the simple tests described previously. To perform lever-out tests, a controlled eccentric load is applied. Markel et al. loaded the cup with a platen on a side of the rim[46]. The maximum load necessary to distract the cup was measured. Similarly, other authors adopted this approach. To increase the reproducibility of the test, some authors adopted a setup composed by a shaft rigidly fixed at the cup dome able to transfer a tangential load through a cable fixed at his free edge and an adjustable pulley used to create the lever arm. Lever-out tests are usually performed to investigate the acetabular stability in terms of implant friction effects and/or impingement effects[22,23,37,38,44,45,47,48,49,50,52,55,56,57,58,61,62,63].

Phisiological test

Physiological tests try to overcome the limitations of simple tests related to the imposed direction of cup migration, in order to be more consistent with the real scenario. It is

important to underline that "physiological" must not be intended as the simulation of the entire load spectrum that the cup withstands *in vivo* during a specific activity, but the simulation of a simplified loading configuration with one or a few fixed directions that are representative of a particular motor task. Such fixed load direction is normally represented by the direction of the load peak measured *in vivo* during a specific motor task performed by patients implanted with a telemetric device[77,78]. In order to reproduce the proper loading configuration, specimens are aligned with respect of the direction of load. In case of anatomical models (both synthetic and biological), the alignment is provided by constraining the specimen at the sacro-iliac joint, so as to simulate the mechanical boundary conditions of the pelvis. This is done through a vice[67] or in most of the cases with bone cement[26,27,28,39,42,53,54,59,65]. The pubic symphysis is usually kept unconstrained, but in a few cases a support is added to avoid excessive bending of the specimen during the test[27].

1.4.5 Measurement of implant/bone motion

In order to assess primary stability, the relative motion between the cup and the underlying bone during the application of one or more loading configurations has to be measured. As the relative motion is a combination of three-dimensional rotations and translations, to be able to measure separately each component of motion is of outstanding importance. Moreover, as hip bone faces high deformations during the load application[68,79], strains measurements may provide additional information about cup stability.

Despite the previous consideration, most of the studies estimated cup stability by monitoring the mechanical outputs of the testing machine, i.e. the force necessary to distract the cup, the cup resultant migration after the application of a certain load or a single component of translation only. Such approach was frequently adopted in comparative studies where PU foam blocks were used however, the 3D relative motions between the implant and the surrounding bone were not measured as well the periacetabular strains. To have an accurate measurement of displacements and strains, external mechanical sensors must be adopted.

Pointwise mechanical sensors

Over decades the measurements of the cup displacement were taken by mean of pointwise sensors. They are constituted by linear displacement transducers, such as LVDTs[24,30,32,33,35,38,59] or eddy current transducers[40,53,54], that are rigidly fixed on the specimen surface while the sensing probe is kept in touch with the prosthesis. In a few studies a single sensor was used, limiting the measurement of the 6 components of the implant/bone displacement to a single component. To obtain 3D measurements, clusters of 3 sensors were placed around the acetabulum[30,53]. This approach could provide relative out-of-plane translations and rotations, but in-plane motions could not be measured. To overcome this limitation in a few studies a cluster of at least 6 sensors was adopted. Sensors were placed directly in touch with the implant or with a structure integral with the implant and orthogonal to each other so as to obtain 3D measurements referred to a defined reference frame (usually the cup reference frame) [24,32,33]. Even though these sensors are extremely accurate and precise, they are intrinsically limited by their pointwise nature, that may introduce high errors in the measurements of bone displacement, especially in case of large deformations. Secondly, deformations cannot be measured. Crosnier et al. tried to reduce this limitation by measuring the elastic deformation of the bone in a single direction, using two LVDTs placed close to the acetabular rim and in touch with the bone substrate[32,33].

Strain gauges could provide accurate pointwise strain measurements without measuring implant motions. However, to the Author's best knowledge, in no studies they were used in combination with pointwise displacement sensors for the assessment of cup stability. Conversely, they were frequently used to validate finite element models[68].

Optical sensors

Optical measurement techniques allow to measure the 3D implant/bone motions and/or bone deformations by tracking the specimen (implant and bone) or by tracking markers applied on the implant and on the surrounding bone. A laser tracking system was sometimes adopted to obtain a limited number of implant or bone motion component even in combination with strain gauges[46,65]. Alternatively, optical tracking markers were used, similar to those adopted in motion analysis[39]. Due to the limited space for markers

application and their spatial encumbrance, the number of adoptable markers is restricted. Thus, as tracking systems generally calculate the 3D motion by the fitting of the positions measured by each marker, such restriction may affect the measurement accuracy. To overcome this limitation, in some studies, a huge number of small markers were used, whether inserted or stuck in the acetabular insert, rim and in the periacetabular bone[22,26,27,28,29,62]. Even if this technique provided 3D motion measurement with high accuracy and precision, strains were not measured.

The Digital Image Correlation (DIC) technique is an optical technique that can overcome all the previous problems[80,81]. Through the DIC, 3D measurements of displacement and strain measurements over the surface of the specimen can be obtained. A few studies adopted this technique to measure the strain distribution in composite hemipelvis specimens under the application of simple loading configurations[68,79] but, to the Author's best knowledge, no studies were performed so far to assess primary stability of acetabular implant using DIC.

1.5 Aims and outline of the project

The aim of the project was to develop and apply reliable *in vitro* methods to assess the hip acetabular stability in case of primary and revision reconstructions and in particular to:

1. Create a robust reference frame for the human hemipelvis;
2. Develop a reliable method to assess the hip acetabular stability through Digital Image Correlation;
3. Compare the effect on cup stability and periacetabular strains of walking and standing up motor tasks;
4. Compare the effect of the implantation technique on the primary stability of press-fit cups;
5. Compare the effect on cup stability of the use of human bone graft or synthetic bone graft to reconstruct acetabular defects in revision surgery.

The overall project follows a linear structure: after the analysis of the state of the art, two methodological studies were conducted to overcome the limitations of the previous

biomechanical testing on hip acetabular stability (see par. 1.4) and build strong foundations for the following steps. Three clinical problems were investigated thereafter.

In Chapter 2 a reliable reference frame for the human hemipelvis specimens is presented. The definition of the reference frame is fundamental for the interpretation of the results, but it is often neglected in the *in vitro* applications probably because of the difficulty in the transposition from the theoretical model to the practical implementation. Moreover, in the specific case of the pelvis, all the existing theoretical models define the anatomical reference frame starting from anatomical landmarks belonging to both sides of the pelvis. This may constitute a problem in the i*n vitro* implementation, as in most cases hemipelvis specimens are adopted. For this reason, I developed a reference frame for the human hemipelvis based (1) on the same anatomical landmarks used to define the pelvis reference frames and (2) anatomical measurements taken on clinical images. Furthermore, I developed a practical method to apply this theoretical model to the physical specimen.

Chapter 3 presents the method I created to assess the stability of acetabular implants with the Digital Image Correlation measurement technique. This method is accurately outlined in all its steps, starting from the specimen preparation until the elaboration of the DIC measurements. The method was validated with synthetic hemipelvis models in order to reduce the effect of the anatomical variability on the measurement error.

With these two studies a reliable methodological basis was constituted. Due to the versatility of the DIC technique, this method may be applied in a wide variety of clinical topics. For the purpose of the present project, I was asked to investigate clinical problems by suggestions of European experienced surgeons, collaborating with my activities.

In Chapter 4 I compared the effect of different simulated motor tasks on the acetabular stability. To date, *in vitro* studies assessed the acetabular stability by the simulation of walking motor task (assumed as the most common patient activity) or standing. However, looking at the forces acting within the acetabulum during common activities of post-op patients, it results that both walking and standing may not represent the worst-case scenario to investigate if compared to other activities recommended for the patient rehabilitation. For this reason, I developed this study to evaluate which are the differences in terms of implant motions and periacetabular strains in case of walking and standing up

from seated, providing also a clinical interpretation of the implant migration by the comparison of the DIC measurements with radiographical measurements.

Chapter 5 presents a comparison between two implantation techniques adopted in primary acetabular reconstruction. The first technique is more conservative and aims to restore the native hip centre of rotation, while with the second one the implant is medialized until it touches the inner cortical surface of the pelvis. Both the techniques are clinically accepted, but their efficiency in terms of implant stability is based only on theoretical models or surgical experience. In this study, I quantified the effect on cup stability due to the use of such techniques through a biomechanical *in vitro* analysis.

In Chapter 6, a study related to the effect on implant stability of different acetabular reconstruction techniques adopted in revision surgery is reported. In clinical practise, revision surgery of the acetabulum is usually accompanied with bone defects that must be reconstructed before the insertion of the revision implant. Such reconstruction can be performed either with human bone graft or synthetic bone substitute. Although the biological properties of human and artificial bone were deeply investigated, their mechanical effect on implant stability were barely studied. For this reason, I developed an *in vitro* study to compare how the acetabular reconstruction with either human or synthetic bone affect the cup motions and periacetabular strains.

Chapter 2:

Standardization of hemipelvis alignment for *in vitro* biomechanical testing

From the journal paper:

Morosato F, Traina F, Cristofolini L. Standardization of hemipelvis alignment for in vitro biomechanical testing. *J Orthop Res*. 2018;36(6):1645-1652. doi:10.1002/jor.23825[82]

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2.1 Abstract

Although *in vitro* biomechanical tests are regularly performed, the definition of a suitable reference frame for hemipelvic specimens is still a challenge. The aims of the present study were to: (i) define a reference frame for the human hemipelvis suitable for in vitro applications, based on robust anatomical landmarks; (ii) identify the alignment of a hemipelvis based on the alignment of a whole pelvis (including right/left and male/female differences); (iii) identify the relative alignment of the proposed *in vitro* reference frame with respect to a reference frame commonly used in gait analysis; (iv) create an *in vitro* alignment procedure easy, robust and inexpensive; (v) quantify the intra-operator repeatability and inter-operator reproducibility of the procedure. A procedure to univocally identify the anatomical landmarks was created, exploiting the *in vitro* accessibility of the specimen's surface. Through the analysis on 53 CT scans (106 hemipelvises), the alignment of the hemipelvis based on the alignment of a whole pelvis was analyzed: differences between male/female and right/left hemipelvises were not statistically significant. To overcome the uncertainty in the identification of the acetabular rim, a standard acetabular plane was defined. An alignment procedure was developed to implement such anatomical reference frame.

The intra-operator repeatability and the inter-operator reproducibility were quantified with four operators, on male and female hemipelvises. The intra-operator repeatability

was better than 1.58°. The inter-operator reproducibility was better than 2.08°. Alignment in the transverse plane was the most repeatable. The presented procedure to align hemipelvic specimens is sufficiently robust, standardized and accessible.

Keywords: anatomical reference frame; in vitro alignment; biomechanical testing; hemipelvis; acetabular plane

2.2 Introduction

Reference frames and landmarks are of paramount importance in biomechanics[83,84] to allow comparisons between different clinical, numerical, or *in vitro* studies. Standardization of the reference frame is extremely important for *in vitro* biomechanical tests[84,85,86,87,88]. It enables the correct alignment of the specimen and applied loads, in order to reproduce a physiological loading condition. With the definition of reproducible testing conditions, it is possible to compare different datasets of different studies.

Reference frames and landmarks for the pelvic bone are adopted in different applications[83,84,89,90,91,92,93,94,95,96]. Reference frames used for the analysis of medical images are qualitative in most cases[89,90,91]. In example, to evaluate the pelvic tilt and sacral slope surgeons generally use lateral radiographs, in combination with anatomical landmarks, assuming that the X-ray frame is aligned with the anatomical planes. However, identification of these landmarks depends on multiple factors like image quality and the position assumed by the patient. For this reason, information that can be extracted from medical images is extremely operator-dependent. *In vivo* applications (i.e., gait analysis) deal with reference frames defined by palpable anatomical landmarks[83,92,93]. Landmarks routinely used in clinical practice are the most accessible ones, while those that would cause patient discomfort are avoided (e.g., pubic tubercle). Identification of the landmarks is heavily affected by the presence of soft tissue.

These considerations dictate some constraint to the reference frames that can be adopted for *in vivo* applications. Surgical navigation adopts reference frames both for the pre-operative planning and for intra-operative deployment[94,95,96]. Similarly, *in silico* applications rely on mathematical models derived from CT scans. Due to the possibility to "navigate" the bone, identification of anatomical landmarks on CT scans (which

contain more detailed information) is more accurate. All the published reference frames for the human pelvis[86,97,98] rely on palpable landmarks that can be reached non-invasively:

- Anterior Superior Iliac Spine (ASIS) defined as the most prominent point on the iliac surface;
- Posterior Superior Iliac Spine (PSIS) defined as the upper and most posterior point of the iliac crest;
- Pubic Tubercle (PT) defined as a prominent forward- projecting tubercle on the upper border of the medial portion of the superior ramus of the pubis.

The Anterior Pelvic Plane (APP) is most widely used clinically[99,100,101]. It is defined by the ASISs and the PTs. Despite the physiological range of tilt of the APP, it is assumed to be roughly vertical in the standing position (anatomical neutral position, ANP)[102,103].

A dedicated reference frame for *in vitro* biomechanical testing can rely on anatomical landmarks that are accessed directly on the specimen (after the removal of soft tissues). For this reason, *in vitro* reference frames are more robust and less operator-dependent than in vivo ones, in which landmarks need to be identified noninvasively.

Despite the considerations above, only a few studies can be found where a suitable reference frame is defined for the pelvis and hemipelvis[104,66]. It is very important to underline that hemipelvic specimens are frequently adopted for *in vitro* purposes[105,106,107].

All the reference frames described above rely on landmarks over the whole pelvis and cannot be implemented on a hemipelvis alone. Currently, there is no consensus on a specific procedure for aligning a hemipelvis. Hence, in order to define a reference frame for the hemipelvis, it is necessary to determine its alignment with respect to the whole pelvis. The few previous studies dealing with hemipelvic specimens lack detail about its alignment: Lewton[66] specified the direction of loads, defined as angles measured relative to the long axis of the pelvis but no reference frame was defined. Preece *et al.*[108] proposed a practical method based on the ANP; however, more information about the alignment procedure were not stated.

The acetabular plane, which is defined as the plane tangent to the acetabular rim is often used clinically[109,110]. The alignment of the acetabular plane was investigated by Murray[111]. In his work, he identified three definitions for acetabular inclination and anteversion: Radiological, operative, and anatomical. Surgeons usually adopt the orientation of acetabular plane as guide for surgical navigation, since it is easily identified

through clinical imaging[109,110]. The acetabular plane was also adopted in different *in vitro* tests[105,106,107,112]. However, the irregular shape of the acetabular rim makes the identification of this plane subjective[113,114]. Recently van Arkel and Jeffers described an *in vitro* method to align a hemipelvic specimen, based on the reference frame recommended by the International Society of Biomechanics (ISB)[86,104]. The proposed procedure requires first aligning the whole pelvis, using four landmarks; the authors propose a procedure to dissect the specimen to obtain two hemipelvises which preserve the same alignment previously identified for the whole pelvis. The requirement of a whole pelvis as starting point may be a limitation, as sometimes only hemipelvic specimens are available.

The aims of the present study were to:

(1). Define a reference frame for human hemipelvis that relies on robust anatomical landmarks and is suitable for *in vitro* applications.

(2). Identify the alignment of the hemipelvis based on the alignment of a whole pelvis. This includes investigating differences in alignment between right and left, and between male and female.

(3). Identify the relative alignment of the newly proposed *in vitro* reference frame with respect to the reference frame usually adopted in gait analysis.4

(4). Create an *in vitro* alignment procedure for hemipelvic specimens easy, robust, and inexpensive.

(5). Quantify the intra-operator repeatability and interoperator reproducibility of the proposed procedure.

2.3 Material and methods

An overview of the workflow is provided in Fig. 2.1. A practical *in vitro* identification of suitable pelvic landmarks was created. Computed tomography (CT) scans of human pelvises were analyzed to identify the alignment of selected landmarks of the hemipelvis with respect to the whole pelvis. An *in vitro* alignment procedure was developed for human hemipelvic specimens. The intra-operator repeatability and the inter-operator reproducibility of the procedure were measured.

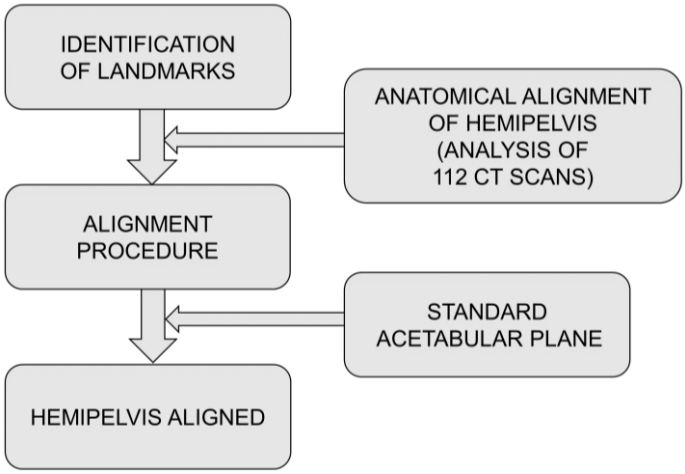

Fig. 2.1: Workflow of the proposed alignment procedure for the hemipelvis

In vitro identification of the landmarks

As shown in different areas, identification of landmarks by palpation leaves a large uncertainty and subjectivity[115]. Direct *in vitro* identification of the landmarks can be more accurate and precise. In order to implement a reproducible procedure, a robust method to identify landmarks, suitable both for pelvis and hemipelvis, was adapted from those commonly used in vivo[86] (Fig. 2.2):

- The iliac and pubic regions must be brought in contact with a plane, while the iliac wing is vertical. ASIS is found as the most external point of the iliac crest, which is in contact against the plane.
- With the bone in the same position, PT is found as the point on the pubic tubercle region, which is in contact against the plane.
- The iliac and ischial regions must be brought in contact with a plane while the iliac wing is vertical. PSIS is found as the most external point of the iliac wing, which is in contact against the plane.

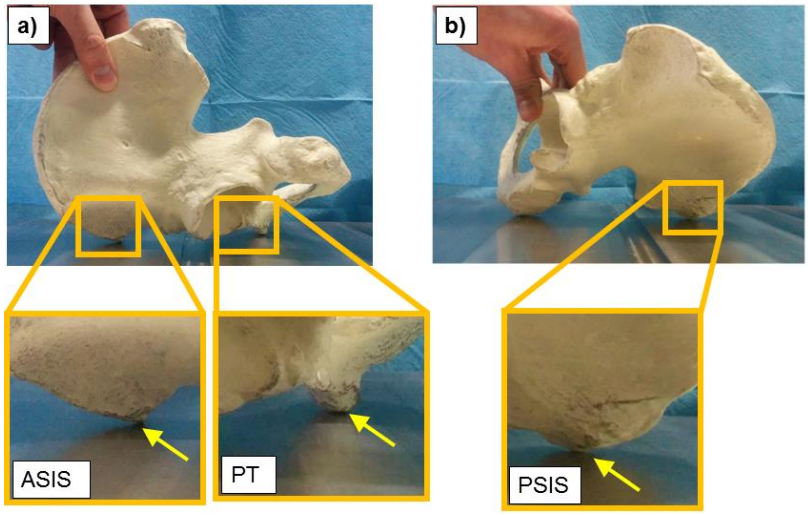

Fig. 2.2: In vitro identification of the landmarks on a hemipelvis: (a) ASIS and PT, (b) PSIS. A left specimen is shown in these pictures.

Identification of the anatomical alignment of the hemipelvis based on the alignment of the whole pelvis, and comparison with ISB frame

In order to adapt to a single hemipelvis the reference frame based on the APP (which is defined for a whole pelvis), the alignment of the hemipelvis relative to the alignment of its respective whole pelvis was identified. Furthermore, the relative orientation of the proposed reference frame with respect to a reference frame commonly used in gait analysis[86] was measured based on the same landmarks. To the Authors' knowledge, this is the first time that similar analysis was made to overcome limitations related to other alignments such as those based on the acetabular plane.

Analysis of Patient CT Scans

Fifty-three CT scans were randomly selected among those taken for hip patients at Istituto Ortopedico Rizzoli between 2014 and 2017. The patients were 25 male and 28 female, 27–88 years old. The scans had a voxel size of 0.7–0.8mm. The scans were imported and analysed through nmsBuilder v1.0[116]. For each scan, the landmarks (ASIS, PSIS, and PT) were identified on the whole pelvis according to the description above. The pelvises were oriented in order to reach the ANP (tolerance 0.1°). To measure the alignment of a single hemipelvis relative to the alignment of its respective whole pelvis, two different angles were measured (Fig. 2.3):

- β: the angle formed by the line connecting PT and ASIS with the transverse plane of the whole pelvis;
- δ: the angle formed by the line connecting ASIS and PSIS with the sagittal plane of the whole pelvis.

In addition, the relative orientation of the proposed reference frame with respect to the ISB reference frame[86] (which is commonly used in gait analysis) was measured in all scans after identifying the mid-point of the two PSIS (mid PSISs): this consisted in a single rotation (ξ), in a sagittal plane (Fig. 2.3).

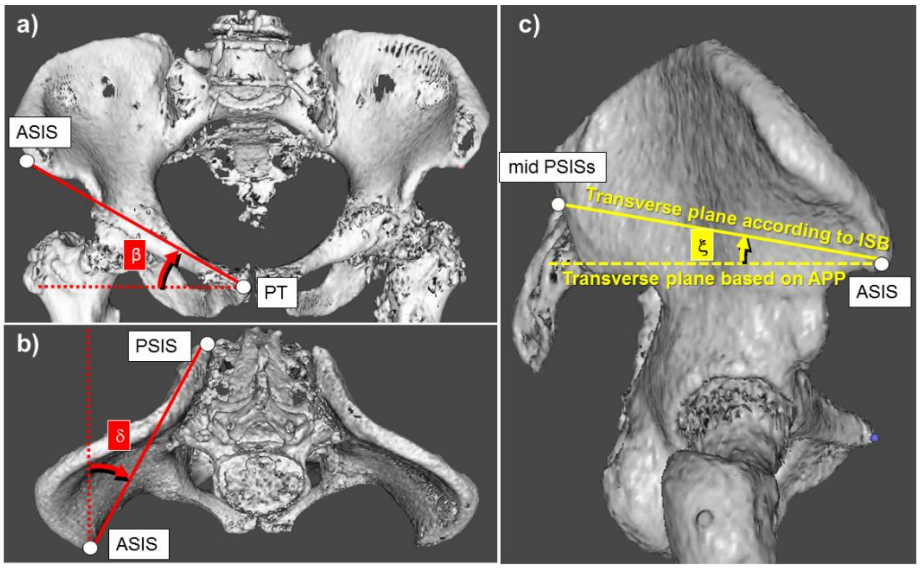

Fig. 2.3: Three different angles were measured in the 53 patient CT scans using nmsBuilder. (a) The angle (β) formed by the line connecting PT and ASIS with the transverse plane of the whole pelvis was measured in a frontal view. (b) The angle (δ) formed by the line connecting ASIS and PSIS with the sagittal plane of the whole pelvis was measured in a transverse plane. (c) The angle (ξ) between the proposed reference frame (based on the APP) and the ISB reference frame was measured in a lateral view.

To exclude outliers, Peirce's criterion was applied[117,118]. Suspect data were checked among subjects, for both angles. To test the procedure, three skilled operators processed three CT scans three time each. To avoid any bias, the scan elaboration was performed on different days between repetitions, so that the operator could not recognize previous elaborations. To assess the intra-operator repeatability (i.e., when the same operator repeatedly elaborates the same CT scan), the standard deviation between the three repetitions was computed, for each of the operators and each CT scan. The repeatability was computed as the root–mean–square–average between CT scans and operators. To

assess the inter-operator reproducibility (i.e., when different operators elaborate the same CT scan), for each of the operators and each CT scan, the average value was computed out of three repetitions. The reproducibility was computed as the standard deviation between the operators.

The significance of differences between the right and left hemipelvises was tested with a paired t-test for β and δ. Differences between male and female for β and δ were tested with an unpaired t-test. A threshold of p=0.05 was assumed. Statistical analyses were performed using MatLab (2009 Edition, MathWorks, Natick, MA).

Alignment procedure for the human hemipelvis

In order to separately control the rotations, the hemipelvises were equipped with a dedicated handle, which was clamped in a 6° of freedom manipulator. The first part of the procedure required aligning the landmarks with respect to horizontal and vertical planes (Fig. 2.4):

- Vertical adjustment: The three landmarks were positioned at the same height (i.e., using an adjustable plate and plasticine);
- Horizontal adjustment: ASIS and PT were positioned parallel to the edge of the reference plane.

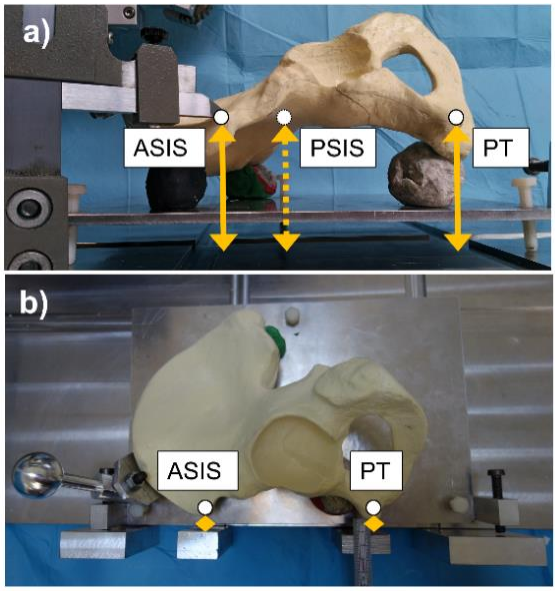

Fig. 2.4: Alignment of a left hemipelvis: (a) Vertical adjustment of the three landmarks. Quasi-frontal view, with the ASIS, PT, and PSIS (hidden by the hemipelvis) at the same height, as measured with the vertical ruler (visible in the far left of the picture). Also visible is the spherical handle mounted on the hemipelvis. (b) Horizontal adjustments of the landmarks. Lateral view of a left hemipelvis with ASIS and PT aligned with the edge of the reference plane.

At this point, the hemipelvis had a known alignment. To overcome the limitations of defining the acetabular plane based on the acetabular rim[111], a standard acetabular plane

was defined (SAP, see Appendix I). With the aim of aligning the hemipelvis with the SAP horizontal, the specimen was subsequently rotated by two angles (Fig. 2.5) (see Appendix I):

- Rotation in the posterior direction by Φ=51°;
- Rotation in the medial direction by Ω=10°.

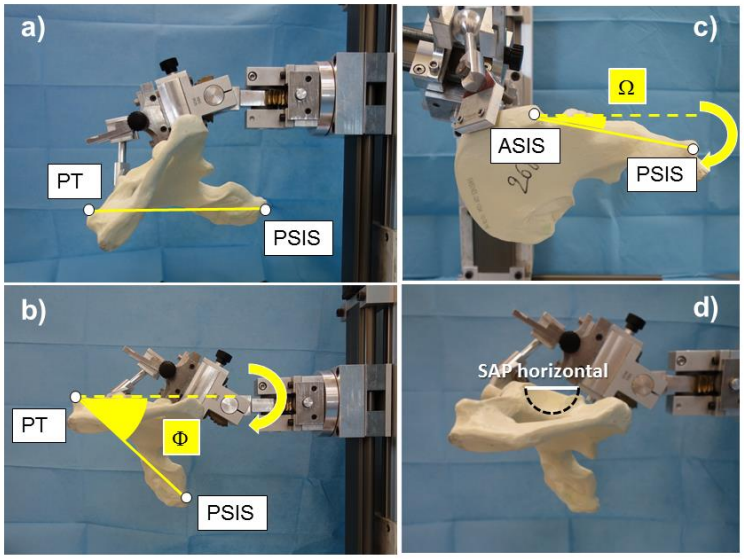

Fig. 2.5: Hemipelvis clamped in the 6° of freedom manipulator through the handle rigidly fixed to the bone. (a) Left hemipelvis viewed from distally (i.e., in quasi-transverse plane) aligned as in Figure 4 and lifted from the plane. (b) Rotation of the specimen by Φ in the medial direction. (c) Rotation of the specimen by Ω in the anterior direction. (d) The standard acetabular plane (SAP) is horizontal once the specimen is aligned.

Assessment of the Intra-Operator Repeatability and Inter-Operator Reproducibility

To test the alignment procedure, hemipelvic bone specimens in solid foam (ERP Mod.1291, ERP Mod.1294, Sawbones, Malmö, Sweden) were adopted. In order to measure the alignment achieved, a squared plastic block was rigidly fixed on the hemipelvises; the absolute orientation of its faces was measured, after the alignment, through a goniometer (Art. 06.07503, IDF, Pontoglio (BS), Italy; precision: 0.1°).

Four operators aligned the two specimens three times each. In order to evaluate the robustness of the procedure, two skilled operators (who performed at least one alignment procedure) and two inexperienced operators were chosen. To avoid any bias, the specimen orientation was modified between repetitions. To assess the intra-operator repeatability, the standard deviation between the three repetitions was computed, for each of the operators and each specimen. The repeatability was computed as the root–mean–

square–average between specimens and operators. To assess the inter-operator reproducibility, for each of the operators and each specimen, the average value was computed, out of three repetitions. The reproducibility was computed as the standard deviation between the operators. Statistical analyses were performed using MatLab.

2.4 Results

Alignment of hemipelvis based on the alignment of whole pelvis

The landmarks could be easily identified in all the CT scans. Based on the Peirce's criterion, five cases were excluded for b and none for d. The intra-operator repeatability was below 0.6° for β, and below 0.5° for δ. The inter-operator reproducibility was better than ±2.6° for β and better than ±3.8° for δ.

The difference between right and left hemipelvises was on average 0.3° for β ($p>0.7$) and 0.2° for δ ($p>0.7$). In none of the 53 pelvises examined, a difference greater than 9° was observed between the left and right hemipelvis for β and δ. The values of β in the female subjects were 0.6° larger than for the males, but this difference was not statistically significant ($p=0.4$, Tab. 2.1). The values of δ were 0.1° larger for the female subjects than for the males ($p=0.9$, Tab. 2.1). The relative orientation of the proposed reference frame with respect to the ISB reference frame in the sagittal plane was on average $\xi=10.7°$. The difference between male and female for ξ was 0.6° and not statistically significant ($p=0.6$, Tab. 2.1).

Tab. 2.1: Values of β, δ, and ξ measured in the CT scans of 53 subjects (Fig. 2.3)

Angles	All	Male	Female	Difference between Male and Female
β	35.5° ± 4.0°	35.2° ± 4.9°	35.9° ± 2.6°	0.6° (p=0.4)
δ	31.3° ± 3.8°	31.4° ± 3.8°	31.3° ± 3.9°	0.1° (p=0.9)
ξ	10.7° ± 5.8°	11.0° ± 6.2°	10.3° ± 5.4°	0.6° (p=0.6)

Average and standard deviation are reported, after excluding outliers, for all subjects, and split by gender. The last column shows the average difference, and statistical significance (unpaired t-test).

Alignment Procedure

All operators performed successfully the alignment, for all the specimens. The time required was about 15 min for each specimen. The intra-operator repeatability was generally below 1.5° for each angle (Fig. 2.6). The inter-operator reproducibility was less than ±2.0° for each angle. Alignment in the transverse plane was most repeatable.

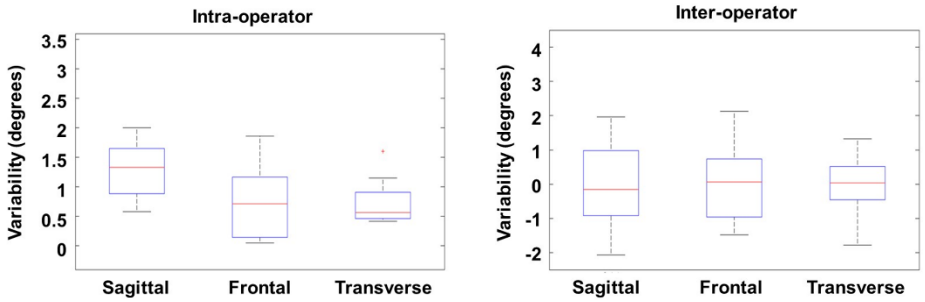

Fig. 2.6: Variability of measured angles on the hemipelvic specimens in each plane: Intra-operator repeatability (top) and inter-operator reproducibility (bottom). The red mark indicates the median; the blue boxes includes the 25–75th percentile; the whiskers extend to the most extreme data points. The outliers are marked with red crosses and were excluded from the analysis.

2.5 Discussion

The aim of this study was to define a reference frame suitable for *in vitro* biomechanical testing of the human pelvis, based on robust anatomical landmarks. As *in vitro* tests are often performed on hemipelvises, the procedure was devised for a hemipelvis (rather than relying on a whole pelvis). To enable comparisons and registrations with other studies, the alignment with respect to a reference frame commonly used in movement analysis was measured. Finally, we aimed at evaluating the reliability of the protocol in terms of intra-operator repeatability and inter-operator reproducibility.

The alignment protocol revolved around anatomical landmarks, which could be accurately identified on the physical *in vitro* specimens. The analysis of 53 patients' CT scans allowed identifying the average alignment of a hemipelvis based on the alignment of its original whole pelvis. No significant differences were detected between right and left sides and between male and female specimens. Furthermore, the relative alignment of the newly proposed *in vitro* reference frame for the hemipelvis was measured with respect to a reference frame commonly used in gait analysis[86]. Thus, even if the rationale

of this study drove us to choose a different reference frame, it is possible to refer our *in vitro* frame to the one used in gait analysis.

When the landmarks were identified *in silico* on CT scans, the intra-operator repeatability was 0.5° in the frontal plane, and 0.5° in the transverse plane; the inter-operator reproducibility was 2.6° in the frontal plane and 3.8° in the transverse plane. When the alignment procedure was applied to physical hemipelvises *in vitro*, the intra-operator repeatability was generally below 1.5°, and the inter-operator reproducibility was less than ±2.0°. The variability mainly depends on the uncertainty in the identification of the landmarks. Due to the limited resolution of the CT scans, it is not surprising that the uncertainty of the *in silico* alignment was worse than the *in vitro* one.

Past studies, where a reference frame was defined for other bone segments (tibia[88] and vertebra[87]), reported errors of the order of 1–3°, comparable to the present one. Only few studies expressly defined a reference frame for the human pelvis *in vitro*[104,66,105,106,107,112,119]. Comparisons with the present study are difficult, as the reproducibility of such references has only seldom been quantified. For instance, Anderson *et al.*[120] performed an *in vitro* alignment of a whole pelvis based on the ASIS and pubic symphysis: While they focused on relative rotations, they did not report the accuracy of their original alignment[120]. A reference frame based on the acetabular plane is often adopted for *in vitro* purposes[105,106,107,112]. However, identification of this plane is complex due to the irregular shape of the acetabular rim[113,114]. To overcome this problem, we defined the alignment for a standard acetabular plane (SAP) based on the advice of a group of hip surgeons.

To the Authors' knowledge, this is the second study in which a reference frame for the hemipelvis was derived from the reference frame of the whole pelvis. In fact, van Arkel and Jeffers developed a procedure to apply the ISB reference frame to the whole pelvis before bisecting it, and then apply the same reference when the hemipelvises were used for *in vitro* testing[86,104]. They found that after bisection, the hemipelvis had a misalignment compared to the original whole pelvis. The error was 1.5±1.6° for the adduction, 0.5±1.1° for the internal rotation, and 0.6±1.7° for the flexion. However, as this error does not include the intra- and inter-operator uncertainty in identifying the landmarks and initially aligning the whole pelvis, the resultant total error of their procedure is larger (i.e., the sum of such errors, and of the uncertainties in aligning the

whole pelvis). Furthermore, for some applications it might be preferable not to drill the large screw holes required to hold the specimen during bisection[104].

The main limitation of our approach is probably that, in order to standardize the reference frame, and to be able to implement it on isolated hemipelvises, we were forced to make a number of simplifications such as applying to any specimen the same average values of the angles. We assumed that the anterior pelvic plane was vertical. However, the inter-subject variability has been reported due to patient's anatomy and pose (i.e., when changing from supine to standing position)[121.122]. Consistently with our aim of standardizing the alignment procedure, we assigned the alignment that corresponds to the average reported in the literature (around 0°[103,122,123]). Similarly, the alignment of the standard acetabular plane was defined based on angle values agreed upon by a pool of surgeons. In principle, the proposed alignment procedure can be implemented also with different angles for the acetabular plane: One just needs to change the final couple of rotations.

The procedure has been tested on synthetic models of the pelvis. To include the variability, both male and female specimens were used. Such models provide detailed anatomy, including the presence and shape of the landmarks. This allowed testing the intra-operator repeatability and inter-operator reproducibility of the alignment procedure. An *in vitro* implementation of a procedure to identify robust anatomical landmarks allows objectively determine the reference points for the alignment. It is important to underline that reproducibility and repeatability of an alignment procedure strongly depend on the identification of the anatomical landmarks; hence practical rules to identify these landmarks should be always taken in consideration for *in vitro* purposes. The reference frame and alignment procedure developed can be applied each time a hemipelvic specimen is studied, both *in vitro* and *in silico*. Furthermore, the proposed reference frame can be easily registered to match a reference frame commonly used in gait analysis. Moreover, the intra-operator repeatability and inter-operator reproducibility quantified in the present study are sufficient for most *in vitro* applications. For these reasons, the presented procedure to align hemipelvic specimens is sufficiently robust, standardized, and accessible, hence can be easily replicated in other laboratories. The proposed reference frame can therefore be assumed as a starting point for numerous pre-clinical *in vitro* tests, for example, to test implant stability of acetabular reconstructions.

2.6 Appendix I: Standard Acetabular Plane (SAP)

To overcome the known uncertainties and limitations of defining the acetabular plane based on the acetabular rim[111], a standard acetabular plane was defined (SAP). Standard values for acetabular inclination (45°) and anteversion (20°) were chosen according to a pool of experienced hip surgeons. Both values are within the Lewinnek "safe zone" (inclination=40°±10°; anteversion=15°±10°)[99], which represents the goal for most surgeons during cup implantation[99,101,124,125]. It was demonstrated that prosthesis implanted within the "safe zone" better resist to dislocation and impingement[99,126].

The angles necessary to align the SAP horizontal were calculated combining the alignment of the hemipelvis based on the whole pelvis, and the inclination and anteversion of the SAP (Fig. 2.7):

- Rotation in a quasi-transverse plane: Φ = Acetabular anteversion + δ = 20° + 31° = 51°
- Rotation in the frontal plane: Ω = Acetabular inclination - β = 45° - 35° = 10°

where:

- β and δ are the average values of the angles measured from the 53 CT scans, to align the hemipelvis based on the whole pelvis.
- Φ and Ω are the final angles to align the hemipelvis with the SAP horizontal.
- All values were rounded to the closest integer.

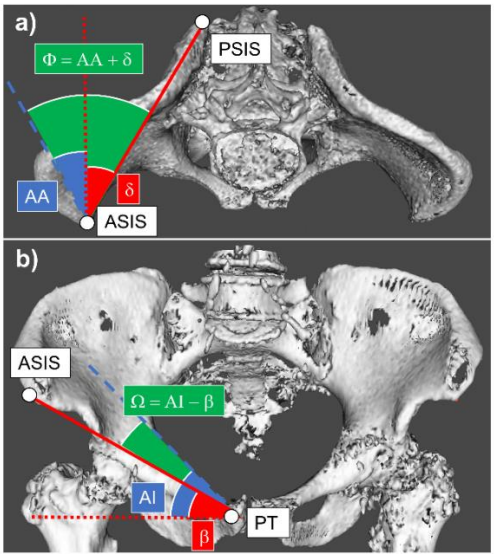

Fig. 2.7: Combination of angles to align a hemipelvis with the standard acetabular plane (SAP) horizontal: (a) Top view of a CT scan of human pelvis showing the angle (Φ), which is calculated as the sum between the angle corresponding to the acetabular anteversion (AA) and d; (b) Frontal view showing the angle (Ω), which is calculated as the difference between the angle corresponding to the acetabular inclination (AI) and b.

Chapter 3:

A reliable in vitro approach to assess the stability of acetabular implants using digital image correlation

From the journal paper:

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3.1 Abstract

The main cause of failure of the hip acetabular component is aseptic loosening. Preclinical test methods currently used to assess the stability of hip acetabular implants rely on crude simplifications. Normally, either one component of motion or bone strains are measured. We developed a test method to measure implant 3D translations and rotations and bone strains using digital image correlation. Hemipelvises were aligned and potted to allow consistent testing. A force was applied in the direction of the load peak during level walking. The force was applied in 100-cycle packages, each load package being 20% larger than the previous one. A digital image correlation system allowed measuring the cup-bone relative 3D displacements (permanent migrations and inducible micromotions) and the strain distribution in the periacetabular bone. To assess the test repeatability, the protocol was applied to six composite hemipelvises implanted with very stable cups. To assess the suitability of the method to detect mobilisation, six loose implants were tested. The method was repeatable: the inter-specimen variability was 16 μm for the bone/cup relative translations, 0.04° for the rotations. The method was capable of tracking extremely loose implants (translations up to 4.5 mm; rotations up to 30°). The strain distribution in the bone was measured, showing the areas of highest strain. We have

shown that it is possible to measure the 3D relative translations and rotations of an acetabular cup inside the pelvis and simultaneously to measure the full-field strain distribution in the bone surface. This will allow better preclinical testing of the stability of acetabular implants.

Keywords: acetabular loosening, biomechanical testing, bone strain, digital image correlation (DIC), hip biomechanics, implant stability, permanent migrations and inducible micromotions, total hip replacement

3.2 Introduction

More than 50% of failures after total hip replacement is associated with the loosening of the acetabular component[10,128,7]. Implant mobilisation can be described as excessive permanent migration (i.e., the non-reversible implant motion that is accumulated over time), excessive inducible micromotion (i.e., the reversible implant motions observed between loading and unloading), or a combination of both. Clinical studies showed that excessive permanent migrations of the cup in the early post-operative period (of the order of 1 mm) are predictive of long-term loosening[19]. Studies on canine models showed that if inducible micromovements greater than 150 μm occur during the first weeks after implantation, fibrous tissue appears at the bone-implant interface, compromising osteointegration. Conversely, micromovements lower than 40 μm allow osteointegration[18,129,16]. It is possible that the strain in the peri-acetabular bone contribute to the success/failure of an implant due to possible bone resorption (due to reduced stress level) or osteonecrosis (due to overloading)[20].

In the clinical practice, implant stability is normally assessed through the analysis of the cup migration in consecutive radiographs. Such approach is inevitably affected by errors due to differences in pelvic tilt and to inter-operator variability[130]. Phillips et al.[131] reported errors lower than 3 mm when assessing cup migration manually on plain radiographs. With Roentgen Stereophotogrammetry Analysis errors are lower than 0.27 mm for the displacements and lower than 0.56° for the rotations. Similar results (displacement errors lower than 0.22 mm and rotation errors lower than 0.53°) were obtained with Ein-Build-Roentgen Analysis (EBRA)[132]. However, even if Roentgen

Stereophotogrammetry Analysis and EBRA provide smaller errors than the analysis of plain radiographs, it is not always possible to adopt such techniques routinely in the clinical practice. Many authors identified the cranial migration of the cup, combined with a sagittal rotation as a clinical predictor for cup loosening[19,130,133,134]. Therefore, to meaningfully quantify implant stability, it is important to measure both translations and rotations for cup stability assessment.

Preclinical testing of the expected failure scenarios is mandatory to prevent clinical failures[135,136]. *In vitro* testing on implant stability can be used to measure the cup permanent migrations and the inducible micromotions with high accuracy and precision. Most authors measured implant stability using linear mechanical transducers to measure implant-bone relative motions at selected locations[35,53,54,59,137,138]. Even if linear transducers are intrinsically very accurate, single transducers cannot be used to measure a combination of large rotations and translations. Crosnier *et al*.[32] measured the three-dimensional micromotions of cup implanted in a block of polyurethane foam using a combination of eight linear variable differential transformers. Such approach provided measurements of all components of translation and rotation with good measurement errors (50 μm for the translations and 0.04° for the rotations). Laser telemeters can be used to measure the cup tilt in simplified tests[46]. As an alternative, stereophotogrammetry can be used to measure implant motion in acetabular revision reconstructions[28,39]. All the techniques described above allow measuring implant-bone motions but do not provide any information about the strain distribution in the host bone.

Digital Image Correlation (DIC) is a good candidate to overcome all the previous limitations, as it provides 3D full-field measurements of displacement and strain with high accuracy and precision[80]. DIC was adopted to measure the strain distribution on the surface of the iliac wing before and after implantation[68,79]. In both papers, the strains measured with DIC were used to validate a finite element model. However, implant motions were not investigated.

The aim of the present study was to devise an *in vitro* test to reliably assess the stability of hip acetabular implants preclinically. More specifically, the procedure must be able to measure:

1. The 3D permanent migrations and inducible micromotions between the cup and the host bone, both in terms of translations and rotations;

2. The distribution of strain in the host bone surrounding the implant.

The method was assessed in terms of measurement errors, repeatability, and suitability to track implant motions in case of both stable and unstable implants.

3.3 Material and methods

We devised a procedure so that it could be applicable both to synthetic and human cadaveric hemipelvises. A reliable reference frame was used for specimen preparation and testing. The mechanical test consisted of a cyclic load of increasing magnitude. The direction of the applied force corresponded to the direction of the peak resultant force during level walking. DIC was used to measure the relative displacements and the strain distribution. Errors affecting displacements and strains were quantified.

Preparation of the specimen

A reliable reference frame for the hemipelvis based on the acetabular plane was adopted[82]. In order to increase the repeatability during preparation and testing, the specimens were potted in an aluminium pot using acrylic bone cement (Fig. 3.1). The hemipelvises were then implanted. To allow the DIC software to properly correlate and track the surface of the implanted specimens, a high-contrast black-on-white speckle pattern was prepared. The implanted specimens were first painted with a white water-based paint (Q250201 Bianco-Opaco, Chrèon, Italy) diluted at 50% with water and sprayed using an airbrush-airgun (AZ3 HTE 2, nozzle 1.8 mm, Antes Iwata, Italy). The black speckle pattern was then sprayed with a water-based paint (Q250201 Nero-Opaco, Chrèon, Italy) diluted at 40% with water (Fig. 3.1). The spraying distance (350 mm) and the pressure (120 kPa) were optimised so as to obtain the recommended mean dot (size 3–5 times larger than the pixel size in the acquired image[80,139]) and to minimise the scatter of dot dimension[140].

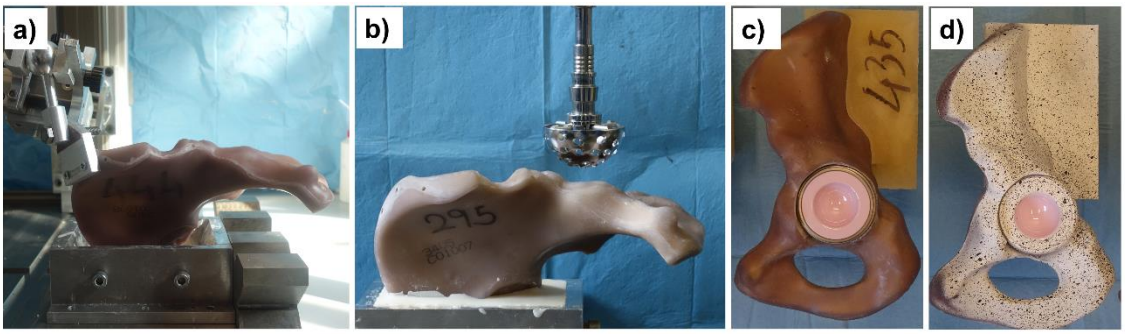


Fig. 3.1: Overview of the preparation of a hemipelvic specimen (left composite bone model): (a) standardised alignment based on anatomical landmarks; (b) reproducible reaming; (c) quasi-lateral view of a specimen implanted; (d) specimen painted with the black-on-white speckle pattern optimised for digital image correlation acquisition

The loading protocol and loading set-up

As the aim was to assess the primary stability of acetabular cups, level walking was simulated as it is the predominant activity in the early post-operative period[141]. Thus, the loading protocol was devised to evaluate the stability of the implant with respect to the direction of the maximum resultant force during level walking. Datasets measured by telemetric implants[77] were used to identify the desired direction. The load datasets were converted so as to obtain the applied force in a reference frame aligned with the acetabular component (with friendly permission of OrthoLoad Club). The test consisted of load packages of increasing magnitude. In each package, 100 cycles were applied at 1 Hz. As the test did not aim to induce fracture, the maximum applied force reached 3 body weight (BW; Fig. 3.2).

The implanted hemipelvis was mounted on an axial servo-hydraulic machine (Mod. 8032, Instron, UK). In order to apply the force in the desired direction, a dedicated wedge was used to mount the specimen on the load cell of the testing machine. Two horizontal low-friction bearings were used to avoid transverse load components (Fig. 3.2).

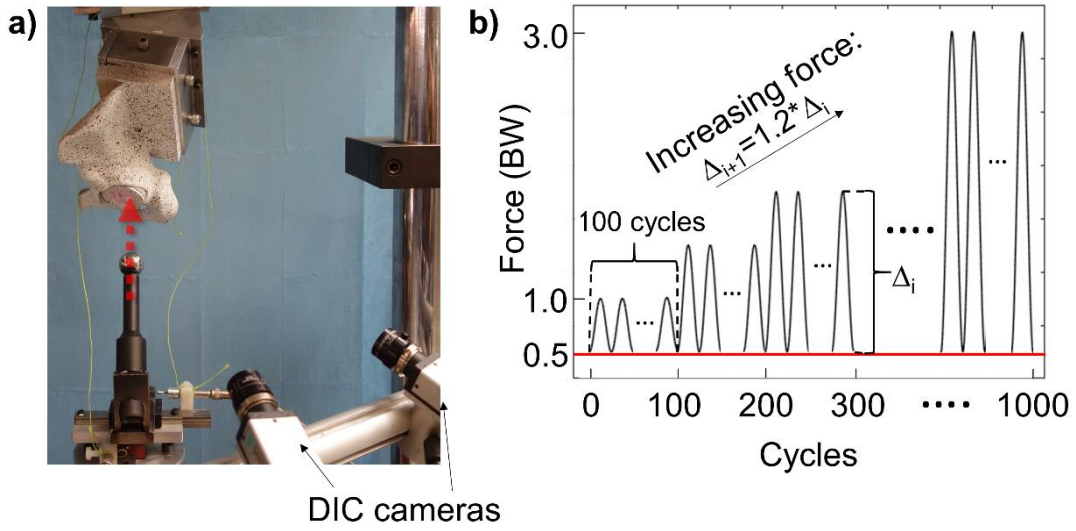


Fig. 3.2: (a) The specimen (left hemipelvis in this case) was mounted in the testing machine with the required alignment with respect to the applied force (red arrow). The two cameras of the digital image correlation system viewed the implanted specimen from a posterolateral view. (b) The plot summarises the loading protocol adopted: 10 load packages were applied, each consisting of 100 cycles

Data acquisition and elaboration

A commercial 3D-DIC system (Q400, Dantec Dynamics, Denmark) was used with a dedicated LED lighting system (10000 lumen in total). Images were acquired by two cameras (5 MegaPixels, 2440 × 2050 pixels, 8-bit) equipped with high-quality metrology-standard 17-mm lenses (Xenoplan, Schneider-Kreuznach, Bad Kreuznach, Germany) for a stereoscopic vision. The cameras were positioned at 300 mm from the specimen, so as to maximise the area framed by both cameras (Fig. 3.2). The field of view was set to 150 × 70 mm (resulting in a pixel size of approximately 0.1 mm), with depth of field of 40 mm (lens aperture f/11). The field of view was wide enough to frame the entire region of interest: the superior aspect of the acetabulum, the posterior column of the hemipelvis, and half of the cup insert. Before each session, calibration was performed using a proprietary calibration target (Mod. Al4-BMB-9 × 9, Dantec Dynamics). The calibration was used to define the reference frame for DIC measurement: In particular, the Anterior Pelvic Plane was selected so as to obtain measurements of displacements referred to a reference frame commonly used in clinics. The correlation was performed with Istra-4D (v.4.3.1, Dantec Dynamics, Denmark). In order to minimise errors in measuring the strain distribution[80], a factorial analysis was performed to optimise the DIC hardware and

software parameters for our specific application (similar to Palanca *et al.*[142]). For our specific instance, the following settings were chosen:

• Frame rate = 20 Hz.

• Facet size = 35 pixels.

• Grid spacing = 27 pixels.

• Displacement smoothing = 3 × 3 pixels (kernel size).

In order to calculate the permanent migrations and the inducible micromotions, the DIC measurements were postprocessed with dedicated scripts in Matlab (2017 Edition, MathWorks, Natick, MA; Fig. 3.3):

1. Two virtual patches were selected on the periacetabular bone and on the cup insert. To reduce operator variability, each patch was generated with controlled dimensions and applied on the specimen so as to cover the same areas.
2. The absolute roto-translation of the bone patch and of the insert patch in correspondence of each load peak, and each load valley was computed through a Singular Value Decomposition (SVD) least squares algorithm[143], assuming the bone and cup insert as rigid bodies.
3. The relative roto-translation between implant and bone was calculated by multiplying the matrices of roto-translation resulting from the previous step. The components of translation and rotation referred to the anteroposterior axis, the craniocaudal axis, and the mediolateral axis were extracted with the Euler angle convention[144].
4. Permanent migration and inducible micromotions were computed similarly to Cristofolini *et al.*[135, 136].
5. The accumulated permanent migration and the 95th percentile of the inducible micromotions during each load package were extracted similarly to Cristofolini *et al.* [135, 136].
6. The first failure criterion was a permanent migration of the cup larger than 1 mm along any axis and/or a tilt of the cup larger than 1° around any axis (such an angle corresponds to an arch of rotation of 1 mm for a 58-mm cup). This is consistent with clinically accepted failure criteria[19].

7. The second failure criterion was a cup inducible micromotion larger than 150 μm along any axis and/or a tilt of the cup higher than 0.3° around any axis (such an angle corresponds to an arch of rotation of 150 μm for a 58 mm cup). This corresponds to the threshold for osteointegration[18,129,16].

In addition, the full-field distribution of the principal strains and the principal directions was computed on the bone surface focusing on the superior aspect and the posterior column (i.e., in the area where the applied force is expected to generate the higher stress, consistently with predictions from previous finite element models[68,79].

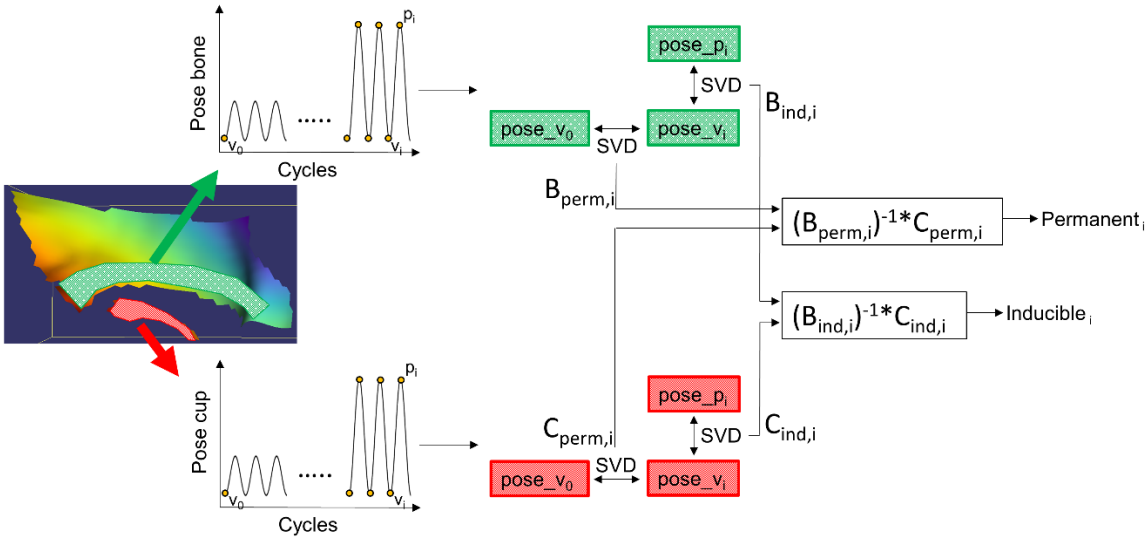


Fig. 3.3: Schematic representation of the analysis of the digital image correlation measured displacements to compute the permanent migrations and the inducible micromotions. The frames in correspondence of the load peaks and load valleys were extracted. The pose of two virtual patches on the bone and on the cup were computed. The roto-translation matrix of the bone-patch (B) and that of the cup patch (C) at each load valley with respect to the first valley (B_{perm} and C_{perm}) and at each load peak with respect to the corresponding valley (B_{ind} and C_{ind}) were computed through a Singular Value Decomposition least squares algorithm. Finally, the relative roto-translation matrixes between the cup and the bone were computed so as to extract the permanent migrations and the inducible micromotions at each cycle

Assessment of the test procedure

In order to quantify the errors of the proposed procedure, a repeatable test bench was used. Six composite hemipelvises (Mod. 3405, Sawbones, Malmö, Sweden) were adopted as bone models. Synthetic bone models are advantageous in the first stages of preclinical testing as they allow reducing the inter-specimen variability. Composite pelvises were used in this stage to quantify the errors of the procedure (without the variability that would be associated with cadaveric ones). Commercial primary acetabular implants (Plasmafit®

Plus NV158T, Aesculap AG, Tuttlingen, Germany) were used. They were implanted under optimal conditions (recommended reaming and full press-fitting) to achieve stable and repeatable implantation. To minimise the cup deformation, ceramic inserts (Biolox® delta NV106D, Aesculap AG, Tuttlingen, Germany) were used. The specimens were prepared with the proprietary reamer to reach a 0.5-mm interference. An experienced hip surgeon implanted the cups following the manufacturer's guidelines: The cup was impacted until the surgeon manually assessed that implant stability was achieved. After implantation, the actual implant alignment was measured and compared with the planned alignment (inclination = 45°, anteversion = 20°). Cups with alignment errors higher than 5° would have been discarded (no specimen exceeded this threshold). To define the loading protocol, composite hemipelvises were assumed to belong to patient with BW = 800 N (Fig. 3.2).

Analysis of the intrinsic errors of the DIC-measured translations and rotations

In order to assess the intrinsic accuracy and precision in measuring the translations and rotations, a rigid 60 × 60 mm target (i.e., similar to the acetabular cup) was painted with the optimal speckle pattern. This target was rigidly translated (10 mm in all directions in 1 mm steps) and rotated (20° in all directions in 1° steps) with respect to a similar stationary target, using a high-precision positioning device (custom-made assembly of a lifting unit (Mod. KULDP20, Misumi, Tokyo, Japan) and three rotary stages (two Mod. RPG110 and one Mod. RPG85, Misumi). The translations and rotations of the moving target with respect to the stationary one were measured with the protocol above (Fig. 3.3) applied to such DIC-acquired images.

Analysis of test repeatability on stable implants

To quantify the repeatability of the full process (from the specimen preparation to measurements elaboration), stable cups were tested first. The expected micromovements for such implants were small; thus, stable cups represented a consistent testbench. In other words, as the inter-specimen output variability derives from a combination of measurement variability and intrinsic inter-specimen differences, performing tests on stable and reproducible implants provided an estimate of the measurement variability

(more precisely, an upper boundary for it). In order to assess the test repeatability, the mean and standard deviation between specimens was computed for the permanent migration and for the inducible micromotion for each of the load packages. Peirce's criterion was applied to detect outliers[118].

Analysis of the DIC applicability on unstable implants

In order to assess the applicability of this DIC protocol to track large migrations and measure large inducible motions (expected in case of implant loosening), the same specimens were modified to mimic a loose implant. The cups were extracted from the hemipelvises, and the acetabula were over-reamed so that the diameter of the cavity was 0.5 mm larger than the cup. A 2 mm thick layer of plasticine was applied in each acetabulum. As this condition is far from the standard surgical protocol, 10 controlled impacts (10 N from a 30 cm height) were used to insert the cup in a consistent fashion. Fixation of the cup was provided by the sinking of the cup in the plasticine layer. Then, the same mechanical test was repeated. To verify if the DIC could track large motions in unstable implants, tests were extended even after exceeding the failure criteria above, until completion of all the load packages.

Analysis of DIC errors (zero-strain test)

In order to quantify the systematic and random measurement errors, a zero-strain test was performed on each specimen, when the optimal parameters were used. A pair of images of the unloaded specimen were captured and analysed with the optimal hardware and software DIC settings in order to assess the measurement uncertainties in a known configuration (zero strain). Being in a zero-strain configuration, any strain different from zero was accounted as measurement error.

3.4 Results

Intrinsic errors of the DIC-measured translations and rotations

The analysis of the roto-translations imposed to the rigid target indicated that the intrinsic errors of the measurement procedure were smaller or equal to the errors of the positioning system (2 μm on the translations, 0.1° on the rotations).

Measurement repeatability on stable implants

Measurements of displacement and strain were successfully obtained for all stable implants throughout the test. No implant failed even with the highest loads (Fig. 3.4). After the application of Peirce's criterion, one specimen had to be excluded (in retrospect, it was noted that this specimen was damaged during implantation). The inter-specimen variability was computed for the permanent migrations and for the inducible micromotions along the anteroposterior axis, the craniocaudal axis and the mediolateral axis. The inter-specimen variability was computed also for the rotations, about the same axes (Tab. 3.1). As expected, higher loads corresponded to larger motions and generally also to higher inter-specimen variability. The variability of the permanent migrations throughout the test did not exceed 10 μm for the translations and 0.04° for the rotations. The variability of the inducible motions did not exceed 16 μm for the translations and 0.04° for the rotations. As expected, the inter-specimen variability was one order of magnitude larger than the intrinsic error of the measurement procedure.

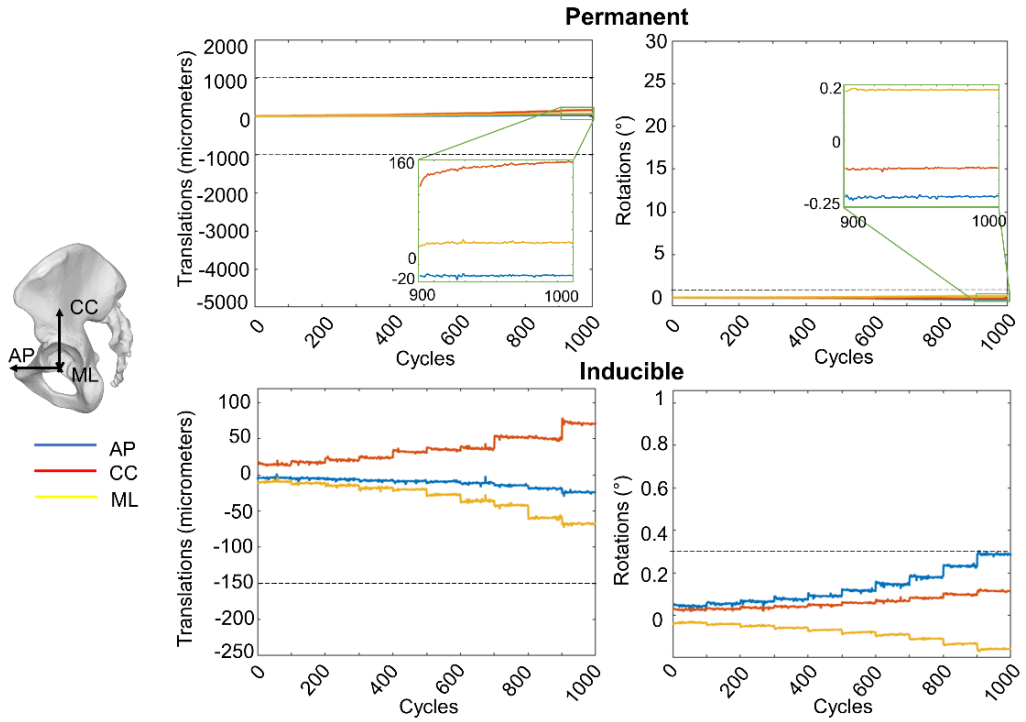


Fig. 3.4: Trend of migrations of a typical stable implant. The three components of translation and the three components of rotation were obtained both in terms of the permanent migrations and of inducible micromotions. To allow comparison, the same scale is used as for the unstable implants (Fig. 3.5). The dashed lines indicate a possible failure threshold for the permanent and inducible translations and rotations: Such thresholds were never exceeded by the stable implants.

Tab. 3.1: Inter-specimen variability for the stable implants along the anteroposterior axis, the craniocaudal axis, and the mediolateral axis and for the corresponding rotations

		Translations (μm)	**Rotations (°)**
Permanent	AP	7	0.02
	CC	10	0.02
	ML	6	0.04
Inducible	AP	2	0.02
	CC	16	0.02
	ML	14	0.04

Note. The largest value of inter-specimen variability observed throughout the test (i.e., among the different load packages) is reported. The top part reports the standard deviation between the six specimens for the permanent migrations, the bottom part for the inducible micromotions.

DIC measurements of implant motions for unstable implants

Despite the very high motions, DIC was able to correlate each frame throughout the entire test and provided measurements of displacements and strains even when the implant motions exceeded the thresholds assumed for failure. As expected, all the implants

prepared to be unstable exceeded the thresholds for translations or rotations previously before completion of the whole test (Fig. 3.5).

- One implant failed during the first load package (when 1.0 BW was applied) with permanent rotations exceeding 2.0°;
- One implant failed during the third load package (1.2 BW applied) with permanent rotations exceeding 1.2°;
- Three specimens failed during the fourth load package (1.4 BW), with permanent rotations in the range 1.2°–2.4°;
- Only one specimen failed during the last package (3.0 BW), with permanent rotation exceeding 1.16°.

In all cases, all the tests were extended until completion of all the load packages, even after exceeding the failure criteria. Throughout all the tests, the highest measured rotation reached 30° whereas the maximum measured displacement was 4.5 mm

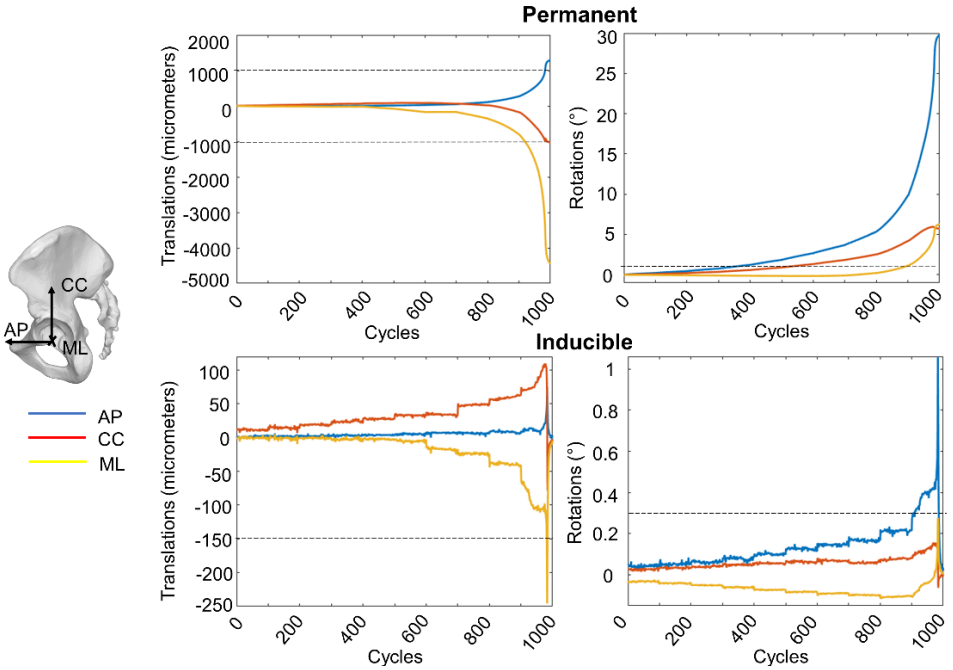


Fig. 3.5: Trend of migrations of one of the unstable implants. The three components of translation and the three components of rotation were obtained both in terms of the permanent migrations and of inducible micromotions. The dashed lines indicate a possible failure threshold for the permanent and inducible translations and rotations: Such thresholds were exceeded by all unstable implants, at different stages during the test

Errors of DIC measurements from zero-strain test

The errors in strain measurements introduced intrinsically by the DIC were estimated measuring the strains in a zero-strain condition (after the optimization of hardware and software parameters). In other words, any strain value different from zero was accounted for as measurement error. As expected, the largest component of error was the random error. The systematic error on the strains on the bone surface in all six specimens was between −6 and +42 με. The random error in all six specimens ranged between 58 and 174 με.

Strain distribution in stable and unstable implants

The full-field distributions of strains were successfully measured in all specimens in the periacetabular bone throughout the test. The highest strains were found in the superior aspect of the periacetabular bone both for stable and unstable implants, with different patterns (Fig. 3.6):

- Stable implants exhibited a high-strain peak near the acetabular rim, in the superior area. In the unstable implants, the highest strains were shifted towards posterior and covered a wider area.
- When 3.0 BW were applied to the stable implants (last load package), the peak value of the maximum principal strain in the periacetabular bone was +1931 με (mean of six specimens, SD = 572 με), whereas the peak minimum principal strain was −1,327 με (mean of 6 specimens, SD = 421 με).
- When 3.0 BW were applied to the unstable implants (only four implants withstood such large loads), the maximum principal strain (ε1) in the periacetabular bone was +2,357 με (mean of 4 specimens, SD = 705 με), whereas the minimum principal strain (ε2) was −1,599 με (mean of 4 specimens, SD = 217 με).
- The mean strain was computed over the patch in the periacetabular bone (Figure 6) with 3.0 BW. For the stable implants, the mean of ε1 was 156 με (mean of 6 specimens, SD = 92 με), whereas mean for ε2 was −100 με (mean of 6 specimens, SD = 80 με). For the unstable implants, the mean of ε1 was +195 με (mean of 4

specimens, SD = 150 με), whereas mean for ε2 was −80 με (mean of 4 specimens, SD = 29 με).

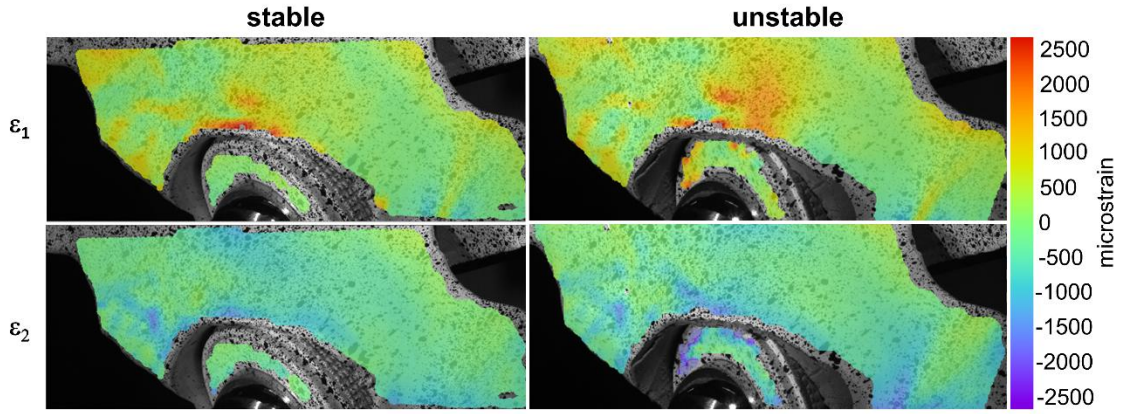


Fig. 3.6: Full-field principal strains measured during a load peak during the last load package (3.0 BW) in one of the stable and one of the unstable specimens. The dashed lines indicate the virtual patch selected on the periacetabular bone. The maximum principal strains (ε1) are plotted in the top images, the minimum principal strain (ε2) in the bottom ones. The largest strains were measured in the superior aspect of the periacetabular bone

3.5 Discussion

In vitro preclinical assessment of acetabular stability can provide measurements of cup micromotion that cannot be obtained clinically with adequate accuracy and precision. The aim of the present study was to devise an *in vitro* test to reliably assess the stability of hip acetabular implants preclinically. As it has been widely highlighted the importance of implant rotation for clinical stability assessment[19], results were not limited to the displacements between the cup and the periacetabular bone but included also the relative rotations. In addition, the strain distribution over the bone surface was measured.

To the author's best knowledge, this is the first study in which DIC was used to assess the implant stability of acetabular implants. To detect the implant mobilisation for increasing loads, cyclic loads with increasing amplitude were applied. The acetabular cup, the posterior column, and the superior aspect of periacetabular bone were framed by the DIC cameras and analysed. The DIC measurements allowed quantifying the spatial relative motions of the cup (three components of translation and three components of rotation), both in terms of permanent migrations and inducible micromotions. In order to reduce DIC measurement errors, a preliminary optimization was performed. This allowed

obtaining small intrinsic errors of the measurement procedure for the implant motions (better than 2 μm for the translations and 0.1° for the rotations). The optimization also allowed minimising the systematic and random errors in measured strains, which were always lower than 174 με. The errors affecting the measured strains were up to five times larger when suboptimal settings were used. It must be noted that the hardware and software optimal settings may be different for different test conditions, different specimens, etc.

Stable implants were tested to quantify the error of the procedure as they represented a reliable testbench. The inter-specimen variability of the optimised protocol under these highly repeatable implanting conditions was very good. Both permanent migrations and inducible micromotions could be measured with an inter-specimen variability smaller than 16 μm for the translations and 0.04° for the rotations. These values are orders of magnitude smaller than the thresholds to predict loosening (1 mm for the permanent migrations, 150 μm for the inducible micromotions). Therefore, the sensitivity of our protocol is sufficient to distinguish between stable or unstable acetabular reconstructions without the need for a large sample size. Unstable implants were also tested, to verify the suitability of DIC in measuring high migrations of the cup. We were able to track cup motions up to 4.5-mm translations and 30° rotations, confirming that even highly unstable implants can be assessed without loss of correlation.

All the measured translations and rotations were referred to the Anterior Pelvic Plane reference frame, so that the measured implant motions can be directly compared with those measured clinically (in fact, most clinical measurements of motions are based on frontal and lateral radiographs[19,130,131]. In principle, our measurement protocol can be modified so as to refer motions to any reference frame, by easily modifying the calibration procedure.

Most previous studies of acetabular stability were based on polyurethane foam blocks and simplified loading such as lever-out[23,145,146], an oblique force[32,41], or a pure torsion[23,74]. Due to their complex morphology, composite models are more representative to evaluate the stability of acetabular implants. Furthermore, most studies above measured only one component of motion (typically a rotation). For these reasons, a direct comparison between our method and these studies is not easy. Tab. 3.2 summarises the measurement errors for the methods adopted in the literature to measure acetabular stability *in vitro*.

Table 3.2: Comparison between different in vitro studies stability of acetabular implants

	Errors on displacements (μm)	Error on rotations (°)	Maximum force (N / BW)	Bone model	Measurement technique
[53]	90	-	2400 N	Cadaveric	Eddy current
[54]	26	-	2390 N	Polyurethane foam	Electromagnetic
[39]	20	-	2250 N	Cadaver	Stereophotogrammetry
[32]	50*	0.04*	2000 N	Polyurethane foam	LVDT
[28]	15	-	0.7 BW	Cadaveric	Stereophotogrammetry
Present study	16	0.04	2460 N (3BW)	Composite	DIC

Note. To estimate the errors of the published methods, the maximum standard deviations of relative bone/cup displacement, and rotation measurements are reported.
Abbreviations: BW, body weight; DIC, digital image correlation; LVDT, linear variable differential transformer.
*Errors are estimated from the graphs provided.

The strain distribution was successfully measured in each specimen, showing the areas of the bone undergoing larger/lower strain. The strain maps highlighted the biomechanical importance of the superior aspect of the acetabulum in load bearing (Fig. 3.6). Due to the reduction in load bearing of the periacetabular cortex, when unstable implants were tested, strains over the bone surface reached higher values if compared with the stable configuration. Moreover, due to the high versatility of the DIC system, in case the region of interest changes (e.g., anterior column), it is possible to study each portion of the specimen by simply adjusting the camera frame.

The errors we found (total error less than 174 με on each component of strain) were slightly lower than those reported in the literature for similar studies. For example, Dickinson *et al.*[79] used DIC to study the strain distribution on implanted hemipelvis when a physiological load was applied and reported an error on the principal strain of 204–224 με. Ghosh *et al.*[68] reported a sensitivity of 145–165 με.

The strains we found in the bone (Fig. 3.6) were within the physiological range of strain for cortical bone (1000–2000 με)[20]. The strain peaks we observed, corresponded to the same region where other DIC-based studies reported the largest strains, that is, in the superior periacetabular aspect[68,79].

It must be acknowledged that for the calculation of the relative roto-translations, both the bone and the cup were assumed to be rigid bodies. We used ceramic inserts so as to make this assumption realistic for the cup. The strains in the periacetabular bone were on

average in the order of 100 με (mean over the patch chosen on the periacetabular bone) when 3.0 BW were applied; thus, the permanent migration and the inducible micromotions could be computed within the assumption of rigid body for the bone. More generally, if higher strains were observed, the method could be easily adapted to exclude regions undergoing high strains when computing bone/cup micromotions so as to minimise the effect of the strain on rigid displacement measurements.

The test was devised so as to apply a simplified loading configuration, under the assumption that due to the small friction coefficient, the resultant joint force would be in a radial direction with respect to the cup/head interface. We focused on a single but critical direction of the force, derived from in vivo telemetric measurements[77]. This simplified loading set-up allowed using the DIC to measure micromotions and strains throughout the test. Alternative methods included multiaxial loading: Such an approach offers the advantage of replicating more complex loading scenarios but would not be compatible with DIC measurements[74].

In the present study, composite bones were used as bone surrogate. This choice was dictated by the need of adopting a highly reproducible test bench, so as to quantify the errors of the experimental protocol. As composite models do not offer the range of anatomy, materials properties, surgical complexity encountered in clinical application, preclinical assessment must include testing on cadaveric specimens. In the future, the very same protocol can be adapted to test implants in cadaveric hemipelvises.

In conclusion, this work has shown for the first time that it is possible to measure the 3D relative translations and rotations of an acetabular cup inside the pelvic bone, both in terms of permanent migrations and inducible micromotions, and, at the same time, to measure the full-field distribution of strain in the bone surface. This has been possible using a combination of biomechanical testing and DIC. This will allow in the future to test the primary stability of acetabular implants, allowing an optimization and preclinical assessment of the device and/or of the implantation technique.

Chapter 4:
Effect of different motor tasks on hip cup primary stability and on the strains in the periacetabular bone: An *in vitro* study

From the journal paper:

Morosato F, Traina F, Cristofolini L. Effect of different motor tasks on hip cup primary stability and on the strains in the periacetabular bone: An in vitro study. *Clin Biomech (Bristol, Avon)*. 2019;70:137-145. doi:10.1016/j.clinbiomech.2019.08.005[147]

The authors wish to thank Clinical Biomechanics for providing the permissions to re-use the manuscript titled *"Effect of different motor tasks on hip cup primary stability and on the strains in the periacetabular bone: An in vitro study"* in the present Ph.D thesis

4.1 Abstract

Background: Excessive prosthesis/bone motions and the bone strains around the acetabulum may prevent osteointegration and lead to cup loosening. These two factors depend on post-operative joint loading. We investigated how *Walking* (which is often simulated) and *Standing-Up* from seated (possibly more critical) influence the cup primary stability and periacetabular strains.

Methods: Twelve composite hemipelvises were used in two test campaigns. Simplified loading conditions were adopted to simulate *Walking* and *Standing-Up*. For each motor task, a single-direction force was applied in load packages of increasing amplitude. Stable and unstable uncemented cups were implanted. Digital image correlation was used to measure implant/bone motions (three-dimensional translations and rotations, both permanent and inducible), and the strain distribution around the acetabulum.

Findings: When stable implants were tested, higher permanent cranial translations were found during *Walking* (however the resultant migrations were comparable with *Standing-Up*); higher rotations were found for *Standing-Up*. When unstable implants were tested, motions were 1–2 order of magnitude higher. Strains increased significantly from stable to unstable implants. The peak strains were in the superior aspect of the acetabulum

during *Walking* and in the superior-posterior aspect of the acetabulum and at the bottom of the posterior column during Standing-Up.

Interpretation: Different cup migration trends were caused by simulated *Walking* and *Standing-Up*, both similar to those observed clinically. The cup mobilization pattern depended on the different simulated motor tasks. Preclinical testing of new uncemented cups could include simulation of both motor tasks. Our study could also translate to indication of what tasks should be avoided.

Keywords: Acetabular hip prosthesis, Primary implant stability, Bone strain, Digital image correlation, Level walking, Standing up

4.2 Introduction

Aseptic loosening is the most frequent cause of failure of the hip acetabular cup[10,128, 7]. Loosening can be predicted clinically by the analysis of the implant migrations in the early post-operative period. This is usually assessed by consecutive plain radiographs (often supported by digital tools such as EBRA) or roentgen-stereo-photogrammetry (RSA)[130,132,133,134,131,19]. As most cups are uncemented[10,128,7], primary stability is important to grant osteointegration (secondary long-term implant stability). In case of excessive interface implant/bone micromotions (i.e. when the inducible motions at each application of load exceed than 150 μm), osteointegration by bone ingrowth is prevented[16,18,148]. In these cases, primary stability is not achieved, and fibrous tissue develops between the loose prosthesis and the host bone, leading to aseptic loosening[17,129]. The load within the acetabulum may affect implant stability and is related to the patient activities[78]. In addition, the strains experienced by the host bone play an important role as alterations in the strain distribution may affect the clinical outcome (i.e. stress-shielding effects and bone resorption)[17,20].

The complex loading in the hip joint is generally simplified in *in vitro* tests, focusing on the hip joint resultant force, in selected motor task(s)[149], often relying on *in vivo* measured forces through telemetric implants[78]. Many experimental *in vitro* studies investigated the relation between implant stability and mechanical features of the cup (e.g. different surface porosity, augmentations, screws)[23,25,37,44,46,63]. In these studies, simplified loading

configurations (e.g. pure torsion[23,25], and lever-out tests[23,37,44,46,63] were applied on simplified specimen, usually constituted by blocks of synthetic or animal bone. In one study, multiple loading configurations were tested: Crosnier *et al*. (2016) used a simulator to replicate different motor tasks by tilting the specimens (polyurethane blocks) around a single axis (maximum range: 5°–40°), while cyclic loading was applied on the cup. No significant differences were found between three different simulated motor tasks on implant motions (translations and rotations).

Synthetic and cadaveric pelvic models are better representative of the anatomy and distribution of material properties surrounding the acetabulum. *Walking* is most often simulated in these cases[27,28,39]. Even if this approach is acceptable (level walking is the predominant activity in the post-operative period[141]), it is possible that such a motor task is not most critical among the daily patient activities. Activities recommended during rehabilitation or early post-operative period include walking, standing up from seated, cycling, climbing upstairs[78,150].

The aim of the present study was to investigate the effect of different motor tasks on the cup primary stability, and on the strain distribution around the acetabulum. Two relevant motor tasks were compared:

- Walking (*Walk*): this was simulated as it is the most common one in hip patients, and most often simulated *in vitro*
- Standing up from seated (*SUp*): this task was selected, among the activities allowed in the early post-operative period, because it induces a large peak force in a completely different direction from the peak during walking[78].

4.3 Materials and methods

Overview and experimental design

To investigate the effect of two different motor tasks among those recommended during the early post-operative period and rehabilitation, an *in vitro* test to simulate level walking and stand up from seated was designed. For each motor task, two test campaigns were made (*Walk* and *SUp*, respectively). Twelve composite specimens were used in total. Six specimens from a previous test campaign (*Walk*) did not require any additional test[127],

but the measurements were re-elaborated so as to be compared with the measurements of the new test campaign (current study, *SUp*) where six specimens were prepared and tested ex novo. Both stable and unstable implants were tested in each campaign. Digital image correlation (DIC) was used to track implant micromotions and measure the strain distribution. As all the twelve specimens were implanted with the same prosthetic component, and were implanted with the same surgical protocol, the implant motions and strains measured in *Walk* and *SUp* campaigns could be compared.

Preparation of the specimens and implantation

To allow long-term simulation of cyclic loading, twelve composite hemipelvis models were used (Mod. 3405, Sawbones, Malmö, Sweden). These hemipelvises consisted of a short-glass-fiber-reinforced shell (replicating the mechanical properties of the cortical bone). The inner part was made of a polyurethane foam (replicating the mechanical properties of the cancellous bone). Each specimen was aligned in a reliable reference frame[82] and potted in an aluminium pot with bone cement.

To prepare the stable implants, each acetabulum was reamed by an experienced hip surgeon until the *lamina quadrilatera* was reached. The reamer size provided an interference of 0.5mm on the radius. Commercial uncemented primary cups (Plasma fit® Plus NV158T, Aesculap AG, Tuttlingen, Germany) were implanted following the manufacturer's recommendations and using the proprietary tools. The surgeon aimed to achieve a standard alignment for the cup (inclination= 45°, anteversion=20°[127]). After implantation, the deviation from the planned alignment was measured. Cups with a deviation higher than 5° would have been discarded (no specimen exceeded this threshold). Ceramic liners (Biolox® delta NV106D, Aesculap AG) were used so as to minimize deformation of the liners and reduce the errors associated with the registration of the cup pose.

After the tests on stable implants, each cup was extracted to prepare an unstable implant in the same specimen. The hemipelvises were over-reamed (1mm on the radius) and a 2mm thick layer of plasticine was inserted in the acetabulum. The extracted cups were re-inserted in each acetabulum by ten controlled impacts (10 N from 30 cm height).

In order to allow the DIC software to properly correlate and track the specimens motion, the implanted hemipelvises were painted with a high-contrast black-on-white speckle pattern. The pattern was optimized for this application[140,127].

Loading protocols

Both stable and unstable implants were tested in both test campaigns (*Walk* and *SUp*, Fig. 4.1). To simulate the two motor tasks, the *in vitro* loading direction was defined so as to replicate the direction of the *in vivo* peak force measured respectively during level walking (*Walk*) and stand up from seated (*SUp*) (open dataset provided by Orthoload-Club[78]).

1. Level walking (*Walk*): the applied force pointed medially and towards the upper part of the anterior column.
2. Stand up from seated (*SUp*): the force pointed medially and towards the lower part of the posterior column.

The potted specimens were mounted in a uni-axial servo-hydraulic testing machine (Mod. 8032, Instron, UK, Fig. 4.1). In order to apply the force with the selected directions, dedicated wedges were created both for *Walk* and for *SUp*. They allowed to properly align the specimen with respect to the actuator of the testing machine. To apply a pure force, two horizontal low-friction bearings were used.

The same loading protocol of Morosato *et al*. (2019) was used. The force was applied in 100-cycle packages (Fig. 4.1). The amplitude of each load package was 20% larger than the previous one. A patient body weight (BW) of 800 N was assumed for the composite specimens. In order to perform a conservative test, the applied force was incremented up to 50% of the peak measured *in vivo* (i.e. 1.5 BW for *Walk* and 2 BW for *SUp*[78]).

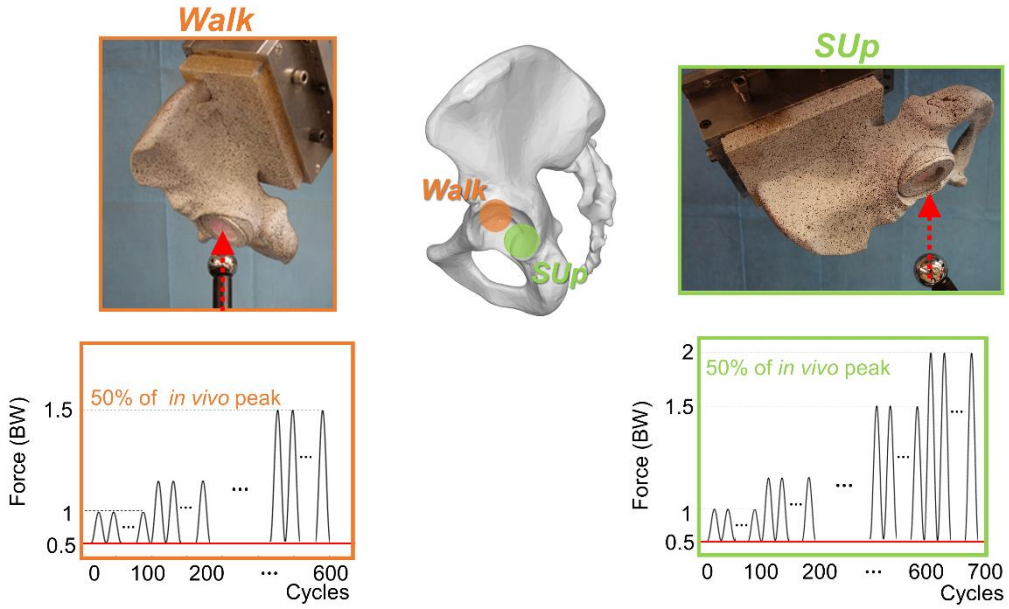


Fig. 4.1: The hemipelvis was aligned so as to apply the force (dashed arrow) in the correct direction respectively to simulate level walking (*Walk*) and standing up (*SUp*). Each load package consisted of 100 identical cycles with a constant baseline (0.5 BW); the peak force of the firs load package was 1.0 BW; the amplitude the cyclic force was incremented by 20% between load packages. The last load package corresponded to approximately 50% of the peak measured in vivo (six load packages for *Walk* and seven for *SUp*).

Measurement of implant motions and strains

A commercial DIC system (Q400, Dantec Dynamics, Denmark) was used to measure the motions of the implant and of the bone and the strains during the test. Two cameras (5 MegaPixels, 2440×2050 pixels, 8-bit) equipped with high-quality metrology-standard 17mm lenses (Xenoplan, Schneider-Kreuznach, Bad Kreuznach, Germany) were used to obtain 3D measurements. The cameras were positioned so as to frame similar regions in the *Walk* and in the *SUp* simulations, i.e. the superior aspect of the acetabulum and the posterior column of the hemipelvis. Such regions corresponded to the most stressed area around the acetabulum, based on preliminary tests. The DIC hardware and software settings were optimized to reduce the random errors affecting the measured strains[142]. For our specific instance, the following settings were chosen:

- Frame rate=20 Hz.
- Facet size=35 pixels.
- Grid spacing=27 pixels.
- Contour smoothing=5×5 pixels (kernel size).
- Displacement smoothing=5×5 pixels (kernel size).

- No smoothing on the strains.

In order to compute the three components of translation and rotation of the implant, the DIC-measured displacements were post-processed through a dedicated Matlab script. The rigid relative motions between the cup insert and the periacetabular bone were computed with a least square singular value decomposition at each load cycle. In particular the permanent migration (i.e. the migration accumulated cycle after cycle), and the inducible micromotion (i.e. the recoverable motion between load peak and valley) were analyzed. A previous methodological study[127] has shown that measurement errors affecting the permanent migrations are smaller than 10 μm (translations) and 0.04° (rotations), errors affecting the inducible micromotions are smaller than 16 μm (translations) and 0.04° (rotations). The following parameters were extracted:

- The permanent migration at the last load cycle of each load package;
- The 95th percentile of the inducible micromotion in each load package.

The maps of the strain distribution on the specimen surface were extracted from the DIC software. The mean and the peak values of the principal strains in the periacetabular bone were analyzed.

In order to quantify the errors of the strain measurements a zero-strain test was performed before each test, when the optimal parameters were used. A pair of images of the unloaded specimen were captured and analyzed with the optimal hardware and software DIC settings in order to assess the measurement uncertainties in a known configuration (zero-strain). Being in a zero-strain configuration, any strain different from zero was accounted as measurement error. The random errors affecting the measured strains never exceeded 150 □m.

Statistical analysis

In order to detect possible outliers, the Peirce's criterion was applied[118] to the measured implant motions and strains. To assess if the effects on implant motions and strains deriving from the application of the two simulated motor tasks were statistically different, a Mann-Whitney test was performed. All stats were performed with Matlab (2017 Edition, MathWorks, Natick, MA).

4.4 Results

4.4.1 Comparison of the implant motions for the two simulated motor tasks

The correlation software was able to track the motions of the bone and of the prosthetic component throughout all tests, both for the stable and the unstable implants, for both test campaigns.

Implant motions of stable implants

After the application of the Peirce's criterion, 8% of the data had to be excluded. Both permanent migrations and inducible micromotions were very small (close to the errors of the measurement chain[127]) in the first load packages. The permanent migration generally increased within each load package and between load packages, and never exceeded 74 μm (translation) and 0.2° (rotation) for *Walk*, and 62 μm and 0.4° for *SUp*. The inducible micromotions showed a generally increasing trend between load packages, and never exceeded 32 μm (translation) and 0.03° (rotation) for *Walk*, and 30 μm and 0.09° for *SUp* (Fig. 4.2). Both the permanent migrations and the inducible micromotions were larger for *SUp* than for *Walk* in terms of rotations, whereas some components of translation were larger for *Walk* than *SUp* (Fig. 4.3). The resultant translations were comparable (not significantly different) between *Walk* and *SUp*. Considering the single components, the largest translation was along the cranio-caudal axis for *Walk* (both permanent and inducible) and along the medio-lateral axis for *SUp*. Significant differences in terms of rotations were found around the cranio-caudal and medio-lateral axes. The largest permanent rotations occurred around the antero-posterior axis in *Walk* and around the cranio-caudal axis in *SUp*.

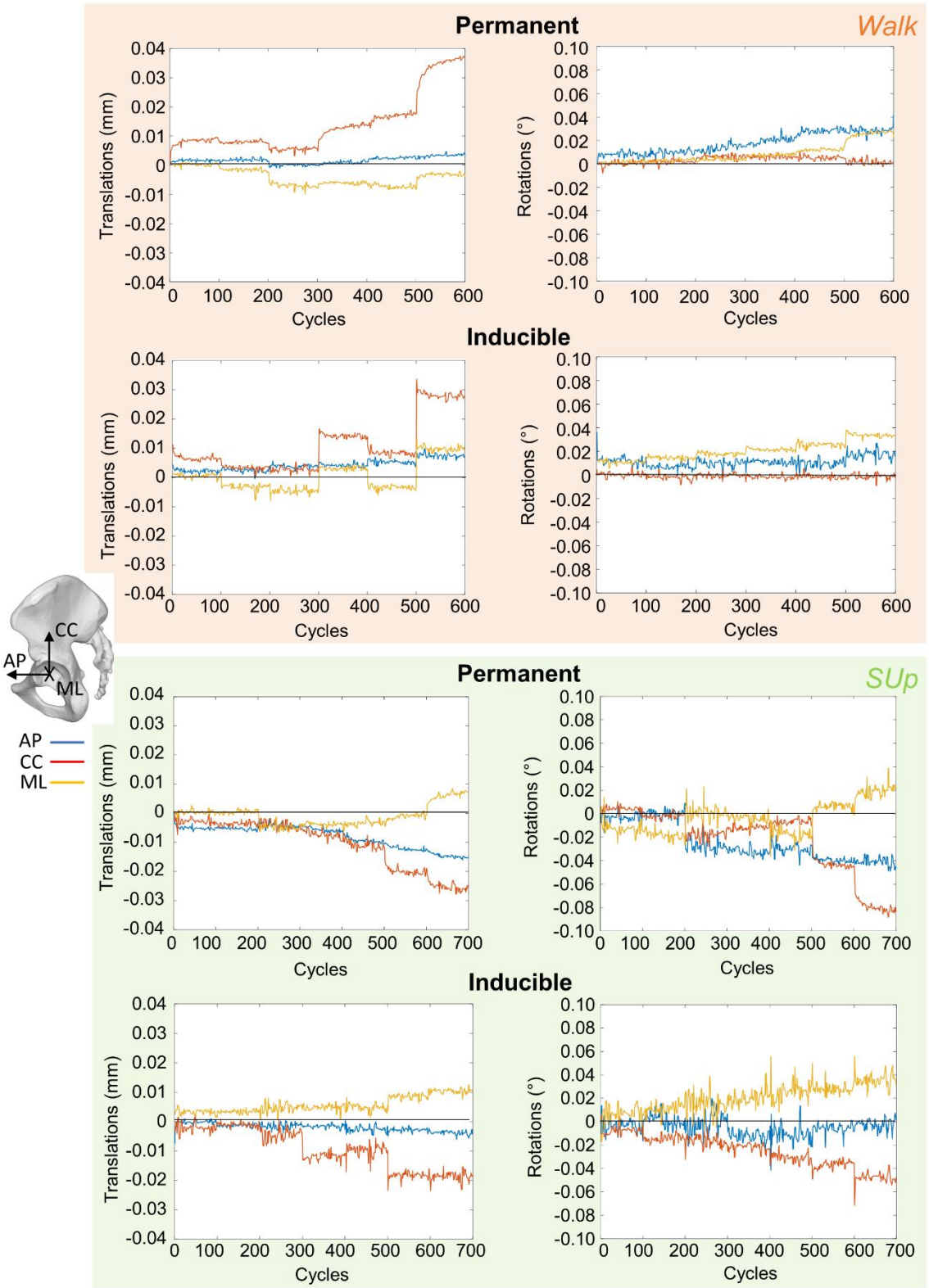


Fig. 4.2: Typical trend of cup motions experienced by stable implants during simulated walking (*Walk*, top) and standing up (*SUp*, bottom). The permanent migrations and inducible micromotions were analyzed in the three components of translation and the three components of rotation with respect to the anteroposterior axis (AP), the cranio-caudal axis (CC) and the medio-lateral axis (ML).

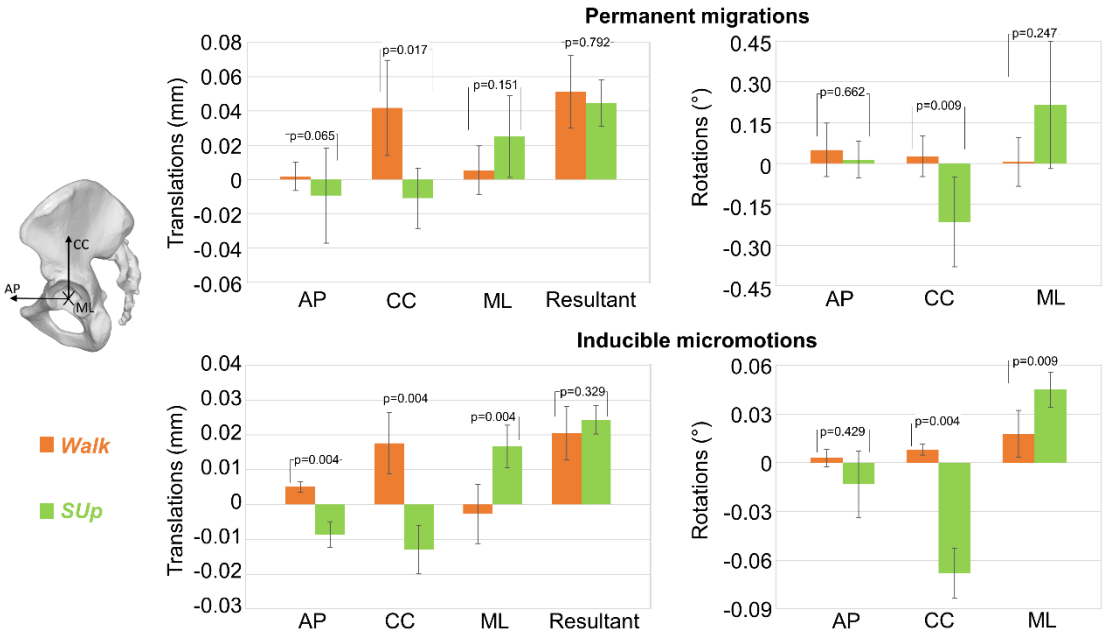


Fig. 4.3: Stable implants: Comparison between cup motions when the largest load was applied during simulated walking (*Walk*) and standing up (*SUp*). The permanent and inducible translations are presented as components along the anteroposterior (AP), cranio-caudal (CC) and medio-lateral axis (ML), and as a resultant. Similarly, the components of rotation around the three axes (AP, CC, ML) are presented. The bars show the mean and standard deviation of six specimens for each motor tasks, after the exclusion of outliers. The P-value from a Mann-Whitney test is also shown.

Implant motions of unstable implants

After the application of the Peirce's criterion, 11% of the data was excluded. The unstable implants faced motions that were 1–2 orders of magnitude larger than for stable implants both for *Walk* and for *SUp*. The motion pattern of the unstable implants varied greatly between specimens with no consistent common trend for the translations and rotations. The permanent migrations increased within each load package and between packages up to 363 µm (translation) and 10° (rotation) for *Walk*, and 843 µm and 2.2° for *SUp*. The inducible micromotions showed a generally increasing trend between load packages, up to 42 µm (translation) and 0.15° (rotation) for *Walk*, and 240 µm and 0.22° for *SUp* (Fig. 4.4). The single components of translation and the resultant translation for *SUp* were significantly larger than for *Walk*. The differences between *Walk* and *SUp* for the permanent rotations showed statistical significance only for the rotations around the medio-lateral axis, whereas all the components of inducible rotations were significantly larger for *SUp* than for *Walk* (Fig. 4.4). The largest rotation occurred around the antero-posterior axis both in *Walk* and in *SUp*.

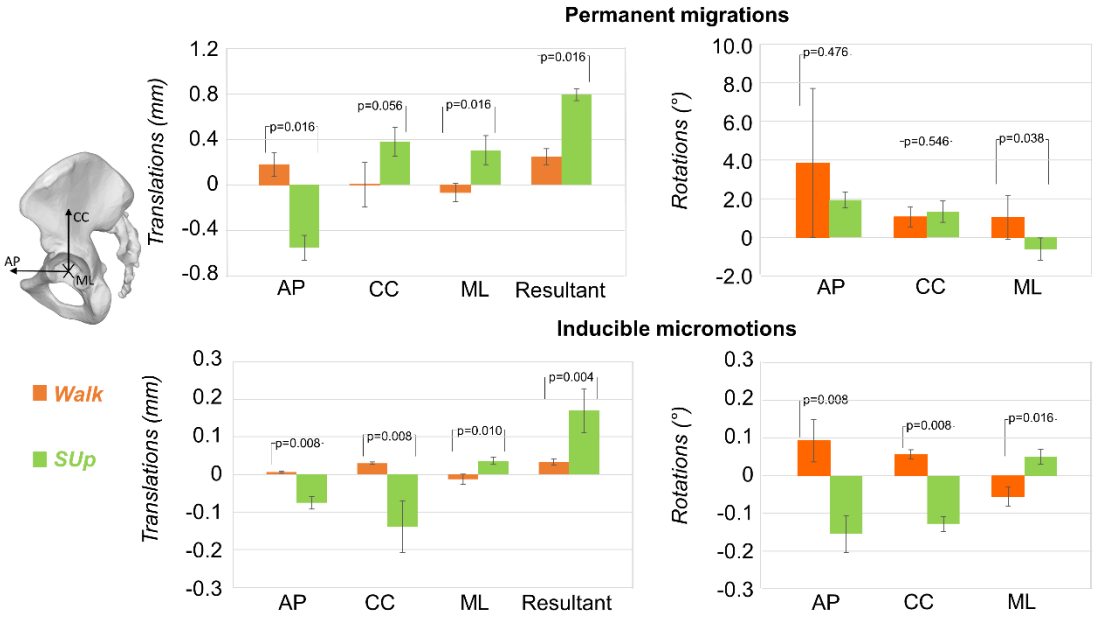


Fig. 4.4: Unstable implants: Comparison between cup motions when the largest load was applied during simulated walking (*Walk*) and standing up (*SUp*). The permanent and inducible translations are presented as components along the antero-posterior (AP), cranio-caudal (CC) and medio-lateral axis (ML), and as a resultant. Similarly, the components of rotation around the three axes (AP, CC, ML) are presented. The bars show the mean and standard deviation of six specimens for each motor tasks, after the exclusion of outliers. The P-value from a Mann-Whitney test is also shown.

4.4.2 Comparison between strain distributions for the two simulated motor tasks

The full-field distribution of strains was successfully measured on the surface of each specimen throughout the tests.

Strains around stable implants

No data had to be excluded according to the Peirce's criterion. The strain distributions around the acetabulum were quite different between *Walk* and *SUp* both in qualitative and quantitative terms (Fig. 4.5). The mean strain over the periacetabular bone when the largest load was applied were significantly higher for *SUp* than for *Walk* (P=0.002 for the maximum principal strain, ε1, P=0.123 for the minimum principal strain, ε2); also the peak strains were higher for *SUp* (P=0.002 both for the maximum and minimum principal strains) (Tab. 4.1). Also the position of the peak strain was affected by the simulated motor task: in *Walk* the largest strains were in the superior aspect of the acetabulum; in *SUp* the largest strains were in the superior-posterior aspect of the acetabulum and in the lower part of the posterior column.

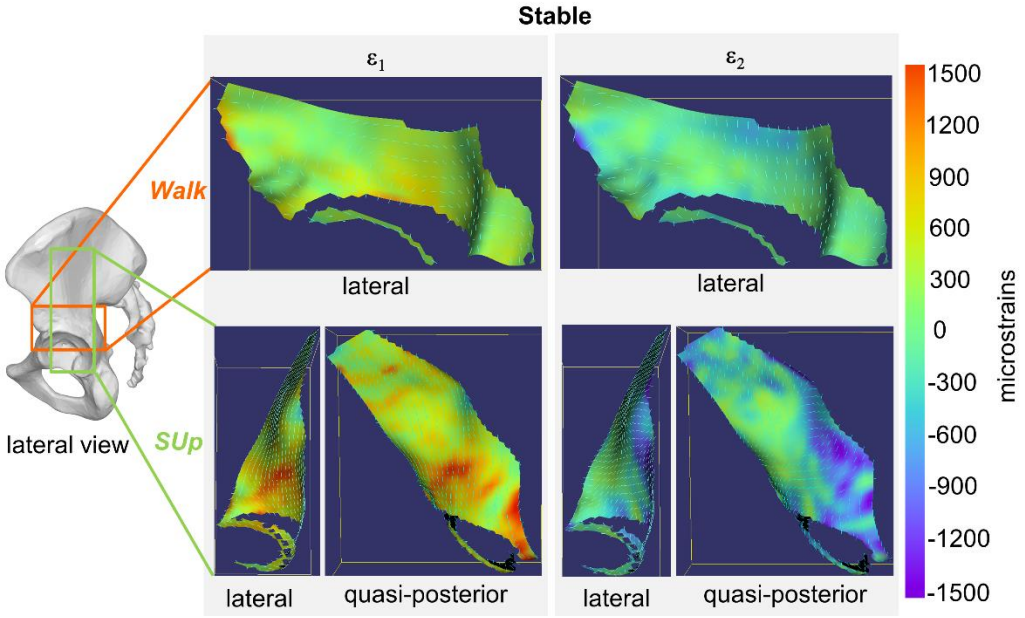


Fig. 4.5: Stable implants: Typical distribution of principal strains measured on the periacetabular bone and on the cup insert when the last peak of load was applied in the simulated level walking (*Walk*, top) and standing up (*SUp*, bottom). The maximum (ε1) and minimum (ε2) principal strains are plotted; the light dashes indicate the direction of the maximum principal strain. For a better visualization of the specimen two different views are provided for *SUp*.

Tab. 4.1: Stable implants: maximum (ε1) and minimum (ε2) principal strains in the bone when the peak load was applied. The mean and the peak in the periacetabular area was calculated for each specimen. Here, the median between the six specimens and the range of the six specimens (after the application of Peirce's criterion for excluding the outliers) is reported.

	Level Walking (*Walk*)		**Standing Up (*SUp*)**	
Principal Strains	**Mean (με)**	**Peak (με)**	**Mean (με)**	**Peak (με)**
ε_1	median = 75 (range = -10 ÷ 120)	median = 638.5 (range = 407 ÷ 722)	median = 415 (range = 410 ÷ 710)	median = 1478.5 (range = 1164 ÷ 1900)
ε_2	median = -65 (range = -90 ÷ 20)	median = -513 (range = -411 ÷ -639)	median = -230 (range = -20 ÷ -380)	median = -1146 (range = -862 ÷ -1845)

Strains around unstable implants

The Peirce's criterion indicated that about 14% of the data had to be excluded due to large differences between unstable implants. Also for the unstable implants, the strain distributions around the acetabulum were quite different between *Walk* and *SUp* (Fig. 4.6). The mean strain over the periacetabular bone when the largest load was applied were significantly higher for *SUp* than for *Walk* (P=0.002 for the maximum principal strain,

ε1, P=0.123 for the minimum principal strain, ε2); also the peak strains were higher for *SUp* (P=0.002 both for the maximum and minimum principal strains) (Tab. 4.2). Similar to stable implants, the peak strain was localized in different areas for the two simulated motor tasks: in *Walk* the largest strains were in the superior aspect of the acetabulum; in *SUp* the largest strains were in the superior- posterior aspect of the acetabulum and in the lower part of the posterior column.

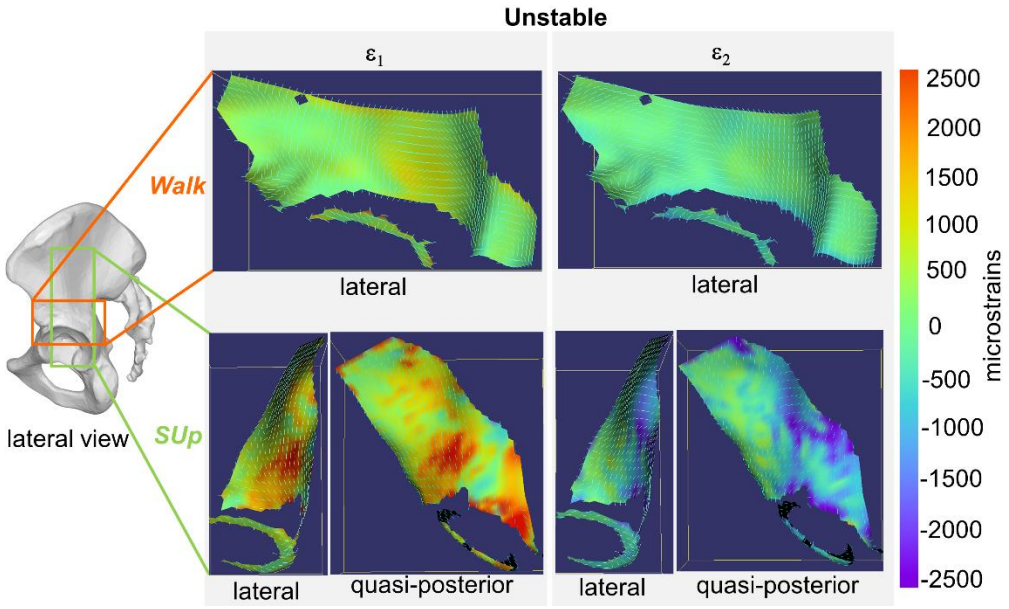


Fig. 4.6: Unstable implants: Typical distribution of principal strains measured on the periacetabular bone and on the cup insert when the last peak of load was applied in the simulated level walking (*Walk*, top) and standing up (*SUp*, bottom). The maximum (ε1) and minimum (ε2) principal strains are plotted; the light dashes indicate the direction of the maximum principal strain. For a better visualization of the specimen two different views are provided for *SUp*.

Tab. 4.2: Unstable implants: maximum (ε1) and minimum (ε2) principal strains in the bone when the peak load was applied. The mean and the peak in the periacetabular area was calculated for each specimen. Here, the median between the six specimens and the range of the six specimens (after the application of Peirce's criterion for excluding the outliers) is reported.

	Level Walking (*Walk*)		**Standing Up (*SUp*)**	
Principal Strains	**Mean (με)**	**Peak (με)**	**Mean (με)**	**Peak (με)**
ε_1	median = 105 (range = 70 ÷ 150)	median = 1021.5 (range = 881 ÷ 1552)	median = 800 (range = 790 ÷ 940)	median = 2309 (range = 2100 ÷ 2916)
ε_2	median = -60 (range = -40 ÷ -160)	median = -876 (range= -773 ÷ -1334)	median = -420 (range = -340 ÷ -540)	median = -1734 (range = -1500 ÷ -2100)

4.5 Discussion

In order to investigate if different post-operative motor tasks affect the cup primary stability and the strains in the periacetabular bone, two biomechanical tests campaigns to simulate (i) a commonly investigated motor task (walking) and (ii) a possibly more critical one (standing up from seated) were performed. Both stable and unstable cups, implanted in composite hemipelvises, were tested for each motor task.

To compare the 3D cup motions and the strain in the periacetabular region, DIC was used. The resultant migrations of stable cups were comparable for *Walk* and *SUp*. However, looking at the single components, walking induced larger cup translations (mainly in the cranial direction), while standing up induced larger rotations (mainly around the medio-lateral axis). These are also the main components of migrations observed clinically. In the unstable implants, *SUp* induced generally larger permanent and inducible translations and rotations than *Walk*.

The principal strains in the periacetabular bone were always larger in *SUp* than in *Walk*. The magnitude of the principal strains increased from stable to unstable implants, exceeding 2300 με (i.e. above the physiological range for cortical bone[20]) when the maximum load was applied in *SUp*. The strain peaks were localized in different regions in *Walk* and *SUp*. Such distribution was generally related to the direction of the applied load (i.e. largest strains were measured in the upper part of the acetabulum in *Walk* and in the lower part of the posterior column in *SUp*), but during standing up large principal strains (comparable to strains peaks) were measured also in the superior-posterior aspect of the acetabulum.

To the Author's knowledge this is the first *in vitro* study in which walking and standing up were compared in terms of 3D cup motions (permanent and inducible translations and rotations), using anatomical models as a testbench. For this reason, a comparison with previous studies is difficult. Moreover, in most past experimental studies and numerical simulations, standing up was not investigated. A direct comparison with the literature can be done only with respect to walking. In two studies[32,33], LVDTs were adopted to measure the 3D implant translations and rotations when walking was simulated with a hip simulator on stable cups implanted in polyurethane blocks. Their results are in line with the *Walk* of the present study: the largest interface motions were caused by cup

translations while the contribution of cup rotations was lower. In Crosnier *et al.*[33], the largest component of permanent translation was 160 μm while the largest component of rotation was around 0.1° (which corresponded to 50 μm of interface slippage). In the present study the largest component of rotation reached 42 μm while the largest component of rotation was 0.05° (0.08° corresponded to 25 μm of interface slippage). While there was a qualitative agreement between the studies, the difference between Crosnier *et al*. and the present study may be explained due the use of different bone models (polyurethane block vs composite hemipelvis) and different loading protocols. Some *in silico* studies found the largest stresses (and consequently the strains) in the superior posterior aspect of the acetabulum[151,152,68,153] during walking. Such results are in line with the strains maps measured by the DIC in *Walk* (Fig. 4.5). The largest strains from a DIC experiment and a validated FE model of an implanted composite reached 600–900 με cranial to the cup[68], which are similar to the largest strain peak measured in this study (Tab. 4.1), for similar loads. In clinical practice, primary stability is normally assessed by the analysis of the cup cranial translation and sagittal rotation (i.e. a combination of the different components of rotation, mainly around the antero-posterior axes) as they represent reliable predictors of cup aseptic loosening[19]. Our approach allowed analysing implant migrations in a way that can be compared to follow-up measurements. In the present study, the largest cranial translation was found for simulated *Walk*, while the largest sagittal rotation was measured in simulated *SUp*. When stable implants were tested, both motor tasks yielded permanent cup translations and rotations that were below the threshold of migration clinically accepted for implant failure (1mm for cranial translation and 1° for sagittal rotation[19]). Moreover, inducible micromotions never exceed 150 μm (i.e. the threshold that prevent the osteointegration[16,17,129,18,148]. Conversely, for the unstable implants both simulated motor tasks induced cup motions that exceeded at least one of the thresholds mentioned above. As these results were obtained in composite bone models, the differences and trends above should be taken in comparative terms.

This study presents some limitations. First of all, a single fixed direction of the force was used for each motor task. This simplification is adopted in many studies[23,25,37,39,42,44,46,53,63,65] and, for our specific case, it allowed DIC to track the specimen and measure cup motions and bone strains throughout the test. In fact, rotating

the specimen would have prevented the DIC cameras from viewing and tracking the cup continuously. Similarly, the muscles were not simulated; muscles implementation is affected by a series of problems (e.g. identification of the insertion point and actuation) that introduce inevitably high uncertainties and costs. For this reason, their effect is normally not included in *in vitro* experimentation.

Simplified boundary conditions were used, constituted by a rigid fixation of the sacro iliac joint. A recent study by Watson *et al.*[154] demonstrated that the constraints at the sacro-iliac joint does not affect significantly the stress distribution in the *ilium*. Conversely, the effect of constraining the pubic symphysis is possibly relevant. As the compliance of the symphysis changes largely between subjects and with age, pubic loading is quite unknown[155]. Due to this uncertainty, and to avoid over-constraining the specimen, the pubic symphysis was unconstrained in our tests.

Composite bone models were prepared with the same protocol for alignment and implantation. This allowed reducing the inter-specimen variability (compared with the cadaveric specimens), thus allowing a direct comparison when the two motor tasks were applied to different specimens. It is possible that implant motions and bone deformations are different in absolute terms in real bone, and also in relation to surgical factors (e.g. reaming, cup alignment, degree of press-fit).

To address the concerns about primary stability, when a new uncemented cup is designed, special attention should be given to the possible modes of loosening. If the prosthesis includes features to enhance stability, this claim should be extensively tested, for the most critical loading configurations. With the present study, we demonstrated that the stability of an uncemented acetabular implant is significantly affected by the simulated motor task. While walking (*Walk*) was more critical in terms of cup cranial migrations, larger rotations were caused by standing up (*SUp*).

Our findings may also provide an indication for post-operative patient activities: for instance, patients where there is a concern for cup tilt (e.g. in association with poor bone support) should receive an indication about which motor task(s) they should avoid.

Chapter 5:

Does cup medialization affect the primary stability of press-fit acetabular cups?

From the manuscript:

Morosato F., Cristofolini L., Castagnini F., Traina F., Does cup medialization affect the primary stability of press-fit acetabular cups? (2020) (*submitted to Bone and Joint Journal)*

5.1 Abstract

Background. Restoration of the native center of rotation (COR) is of paramount importance in total hip arthroplasty. COR reconstruction depends on reaming technique: conventional approaches require more cup medialization than anatomical preparations. To date, the influence of cup medialization on socket stability in cementless implants is still unknown.

Research question. Does cup medialization improve primary stability in press-fit acetabular sockets?

Methods. Five pairs of cadaveric hemipelvises were sequentially reamed using anatomical technique (only subchondral bone removal and COR restoration) and conventional preparation (reaming to the lamina and medializing the cup). A biomechanical test was performed on the reconstructions. Implant motions were measured with digital image correlation while a cyclic load of increasing magnitude was applied.

Results. No significant difference was measured between the two implantation techniques in terms of permanent cup migrations. The only significant difference was found for the cup inducible rotations, where the conventional technique was associated with larger rotations.

Conclusion. Cup medialization does not improve initial cup stability. Considering the influence of medialization on hip biomechanics (loos of bone stock, loss of offset, high stresses at the bone-implant interface and higher polyethylene wear), conventional reaming should not be routinely performed, but only in case of shallow, aspherical cavities after anatomical reaming.

Keywords: Reaming depth; Hip Center of rotation; Cup medialization; implant stability

5.2 Introduction

Restoration of center of rotation (COR) is of paramount importance in total hip arthroplasty (THA)[156,157,158]. An anatomical reconstruction of the COR improves hip biomechanics and function, reduces wear and impingement[156,157]. COR restoration is strongly dependent on the reaming technique[156,158]. The conventional technique aims to the acetabular floor (*lamina quadrilatera*), whereas the anatomical method requires only peripheral reaming, limited to the acetabular rim[159]. Thus, the conventional technique increases cup medialization and may sacrifice a clinically significant amount of acetabular offset, while the anatomical reaming preserves cup medialization and may result in socket under-coverage or overhanging[160,157,158]. To date, the influence of reaming technique (and thus, cup medialization) on stability of cementless press-fit sockets is still unknown. In particular, it is not ascertained if deeper cup positioning may reduce the initial inducible (or elastic) implant micromotions that prevent osseointegration and may lead to cup loosening[16,161,18].

Thus, a cadaveric biomechanical study was designed to compare the effects of two different reaming techniques (conventional and anatomical methods), and consequently, two different cup medializations, on primary stability of press-fit acetabular cups in the same acetabulum. We hypothesized that deeper implantation (conventional technique, more medialization) provided more stable cup implantation. In particular, cup stability was assessed in terms of three-dimensional permanent migrations and inducible micromotions between the cup and the host bone.

5.3 Material and methods

To assess the effect of implantation depth (medialization) on primary stability of press-fit acetabular cups, ten cadaveric hemipelvises were used. Specimens were implanted in two different fashions. First, the cups were implanted after a peripheral reaming technique (anatomical implantation). After the biomechanical test, the specimens were reamed until reaching the *lamina quadrilatera* and implanted with the same cup (conventional implantation). Digital image correlation (DIC) was used to measure the relative 3D implant/bone motion [127].

Preparation of the specimens

Five pairs of cadaveric hemipelvises were obtained through ethically-approved donation programs (Tab. 5.1). This Study was authorized by the Bioethics Committee of the University of Bologna (Prot. 179610 of 7 December 2018).

Tab. 5.1 - List of specimens, including the donors' details, and the size of the implanted cups. The position of cup with respect to the native center of rotation is reported for the anatomical and conventional implantation (negative values indicate that the cup was inserted deeper than the native COR). The last column reports the difference between the two implantations.

Donor	Cause of death	Sex	Age (years)	Height (cm)	Body weight (kg)	BMI (kg/m^2)	Side	Cup size (mm)	Cup center Anatomical implantation (mm)	Cup center Conventional implantation (mm)	Difference between anatomical and conventional implantation (mm)
#1	Sepsis	Female	83	164	63	23	L	56	2.0	-1.8	3.8
							R	56	1.1	fractured	-
#2	Respiratory paralysis	Male	70	175	79	26	L	52	1.3	-2.1	3.4
							R	54	0.9	-2.2	3.1
#3	Unknown	Male	74	176	78	25	L	48	0.4	fractured	-
							R	48	-1.6	-5.6	4.0
#4	Coronary thrombosis	Male	71	187	92	26	L	60	1.7	-1.8	3.5
							R	62	-0.7	-1.8*	1.1*
#5	Cardiac arrhythmia	Male	61	181	96	29	L	56	1.4	-1.6	3.0
							R	54	1.5	-1.6	3.1
Median		**-**	**71**	**176**	**79**	**26**	**-**	**55**	**1.2**	**-1.8**	**3.4**
SD		**-**	**7.9**	**8.5**	**13.2**	**2.2**	**-**	**4.5**	**1.1**	**1.4**	**0.4**

Note (*): this specimen could not be tested because the difference between anatomical and conventional implantation was less than 3 mm.

The soft tissues around the acetabulum and in correspondence of the anatomical landmarks were removed. Each hemipelvis was aligned in a reproducible reference frame and potted in correspondence of the sacro-iliac joint in an aluminum pot with bone cement (Fig. 5.1) [82]. To avoid excessive bending of the specimen during the biomechanical test, a constraint was added in the pubic symphysis (Fig. 5.2).

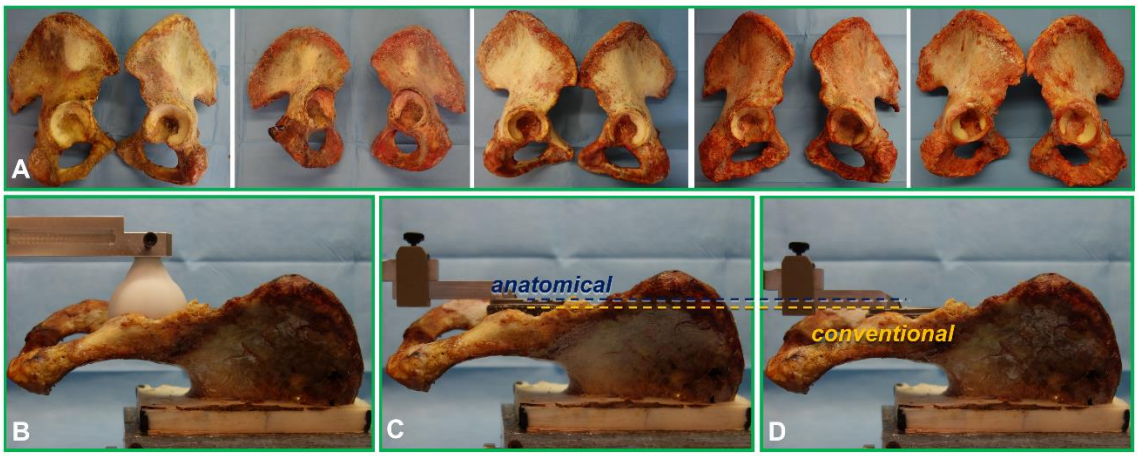


Fig. 5.1: Ten paired hemipelvises from five donors were prepared (A). The size of each acetabulum was measured to plan implantation and to record the position of the native anatomical center of rotation (B). All the specimens were first implanted so as to restore as close as possible the native center of rotation (anatomical implantation, C) and subjected to biomechanical test. The specimens were then re-implanted after reaming towards the *lamina quadrilatera* (conventional implantation, D).

Spherical plugs with controlled dimensions were used to measure the cup size required for each acetabulum, and to estimate the position of the native anatomical COR (Fig. 5.1). An experienced hip surgeon (FT) performed reaming and implantation so as to correctly prepare the hemipelvises according to the two implantation techniques:

- In anatomical implantations, peripheral reaming was performed aiming to restore the native COR as close as possible, with a minimal medialization and circumferential, complete cup coverage. Commercial primary cups (Plasma fit® Plus, Aesculap AG, Tuttlingen, Germany) were implanted following the manufacturer's recommendations. To ensure that cups were within ±2 mm from the native COR, the position of the cup center after implantation was measured (Fig. 5.1) (Tab. 5.1). Ceramic liners (Biolox® Delta, Ceramtec, Plochingen, Germany) were inserted. After the biomechanical test (see details below), the cups were extracted.

- To prepare the hemipelvises for the conventional implantation, each acetabulum was progressively medialized by reaming to the *lamina quadrilateral* (using the same reamer size as in anatomical technique). The same cups were re-implanted. The position of the COR of such conventional implantation was measured and compared with the position of the COR previously achieved with anatomical implantation (Fig. 5.1). A difference of position smaller than 3 mm required the specimen to be reamed deeper (if possible) and re-implanted. In one case it was not possible to ream deeper and the specimen was not tested; two specimens were fractured during re-implantation and were not tested; therefore, 7 specimens were available with both implantation techniques (Tab. 5.1). The ceramic liners were re-inserted and the same biomechanical test was repeated.

As the digital image correlation (DIC) software requires the surface to have a high-contrast speckle pattern, a black-on-white pattern was painted on the surface of each specimen (covering both the periprosthetic bone and the rim of the cup insert) before the biomechanical tests [127].

Biomechanical testing

In order to reproduce a critical loading configuration, standing up from seated was selected among the typical activities of post-operation patients [78]. In fact, it was shown that such motor task generates the highest load peak in the acetabulum compared with other post-op activities [77], and it results in a migration direction of the cup consistent with that observed clinically [147]. In particular, the direction of the peak force measured *in vivo* during standing up from seated was identified from the open dataset by Orthoload Club [77]. The specimens were aligned in the testing machine so as to apply the force in the selected direction (Fig. 5.2). A system of low-friction linear bearings was used to avoid transmission of any other undesired force component. A uni-axial servo-hydraulic testing machine (Mod. 8800, Instron, UK) was used to apply packages of cyclic load with increasing magnitude similar to Morosato *et al.* [147]. To account for the donor's anatomy, loading was scaled according to the donors' body weight (BW). Each package consisted of 50 load cycles. The first load package reached a peak force of 1 BW, the following packages were always 10% larger than the previous one (Fig. 5.2).

As each specimen had to be tested twice (with the two implantation techniques), it was crucial to prevent specimen damage. Therefore, a coarse stop criterion was implemented during the first test session (anatomical implantation) in real time throughout the test: the test was continued (with load packages of increasing magnitude) until the measured cup permanent migration exceeded 0.5 mm. In addition, if the strains measured with DIC (see below) exceeded 2000 με (i.e similar to the physiological deformations experienced by bone [20]) the test was stopped. To allow paired comparisons between the two implant conditions, each specimen was tested after conventional implantation up to the same load reached in the previous testing with anatomical implantation.

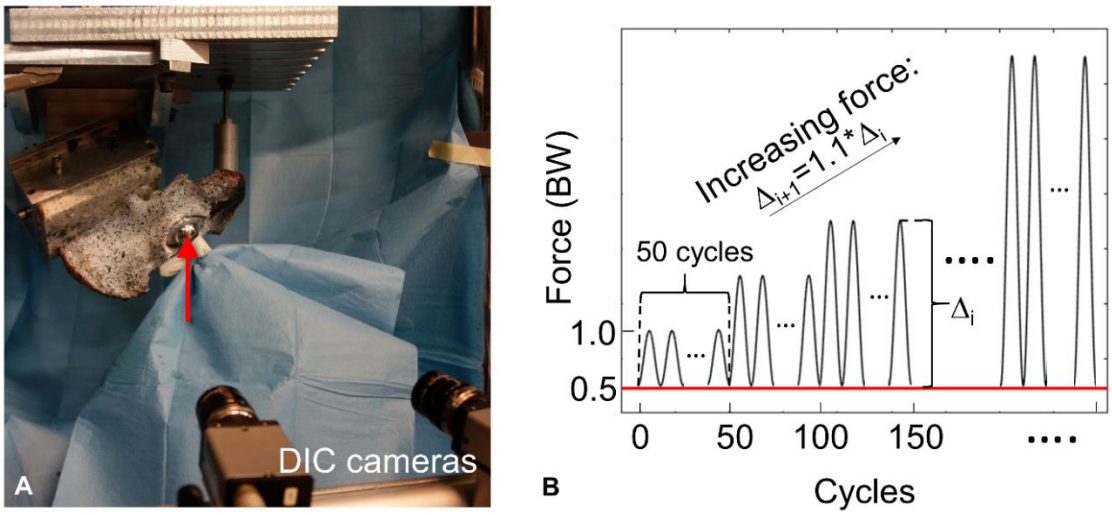


Fig. 5.2: The specimen was mounted in the testing frame so as to apply a force (red arrow) in the selected direction (A); the hemipelvis was constrained through the pot on the sacroiliac joint, and through a support at the pubic symphysis; the cameras of the DIC system were placed so as to frame both the cup and the surrounding bone. Load cycles of increasing magnitude were applied in packages of 50 cycles (B); each load package was 10% larger than the previous one; the force was scaled on the patient body weight (BW).

Measurement of implant motion

A commercial DIC system (Q400, Dantec Dynamics, Denmark) was used to measure the motions of the implant and of the bone throughout the test, following a validated procedure [127]. The system also allowed to measure full-field strains during the test. Two cameras (5 MegaPixels, 2440 ×2050 pixels, 8-bit) equipped with high-quality metrology-standard 17 mm lenses (Xenoplan, Schneider-Kreuznach, Bad Kreuznach, Germany) were used to obtain 3D measurements. The cameras were positioned so as to frame the

implant, the superior aspect of the acetabulum, part of the iliac wing and part of the posterior column (Fig. 5.2).

In order to compute the three components of translation and rotation of the implant, the DIC-measured displacements were post-processed through a dedicated script in Matlab (2017 Edition, MathWorks, Natick, MA)[127]. In particular, the permanent migration (i.e. the migration accumulated cycle after cycle), and the inducible micromotion (i.e. the recoverable motion between load peak and valley) were analyzed.

Statistical analysis

To assess if the effect of the two implantation techniques on implant motions was statistically different, a Wilcoxon signed-rank test was performed using Matlab. The following results were analyzed as paired data (the same load peak was reached for the two implantation techniques in each specimen):

- The cup migration after the application of the last load package in the anatomical vs the conventional implantation.
- The median of the inducible micromotions during the last load package in the anatomical vs the conventional implantation.

5.4 Results

The digital image correlation system was able to track the motions between the cup and the bone throughout the biomechanical tests of the anatomical and conventional implantations.

The permanent translations at the end of the biomechanical test ranged 0.064-0.354 millimeters for the anatomical implantations and 0.065-0.210 millimeters for the conventional ones. The inducible micromotions never exceeded 0.130 millimeters for both types of implantation. The resultant permanent translation was slightly larger for the conventional implantation than for the anatomical one (this difference was not statistically significant, Wilcoxon signed-rank, Fig. 5.3). However, looking at the single components, the permanent translations were slightly larger for the anatomical implantation (again, with no statistical significance). A similar trend was found for the inducible translations, with no statistically significant difference (Fig. 5.3).

The permanent rotations at the end of the biomechanical test ranged 0.001°-0.59° for the anatomical implantations and 0.006°-0.30° for the conventional ones. The inducible rotations never exceeded 0.20° millimeters for both types of implantation. No significant difference was detected between the permanent rotations of the two implantation techniques (Wilcoxon signed-rank, Fig: 5.4). The only statistically significant differences were detected for the inducible rotations around the antero-posterior and around the medio-lateral axis (Fig: 5.4).

A detailed analysis of the individual specimens highlighted that there was no correlation nor visible trend between the difference between the two implantation depths (Tab. 5.1) and the implant motions (both inducible and permanent).

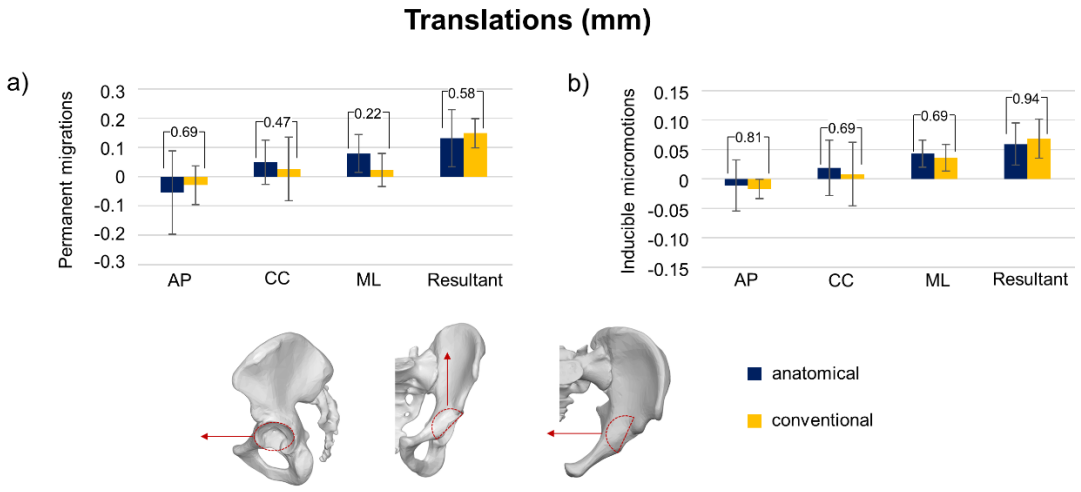


Fig. 5.3: Cup translations when the largest load was applied to the anatomical and conventional implantations. The permanent migrations (a) and inducible micromotions (b) are presented as components of translation along the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) axis, and as a resultant. The three components of cup translation are sketched together with a hemipelvis from the three views. The bars show the median and standard deviation of seven specimens. The *P*-value from the Wilcoxon signed-rank test is indicated for pairwise comparisons.

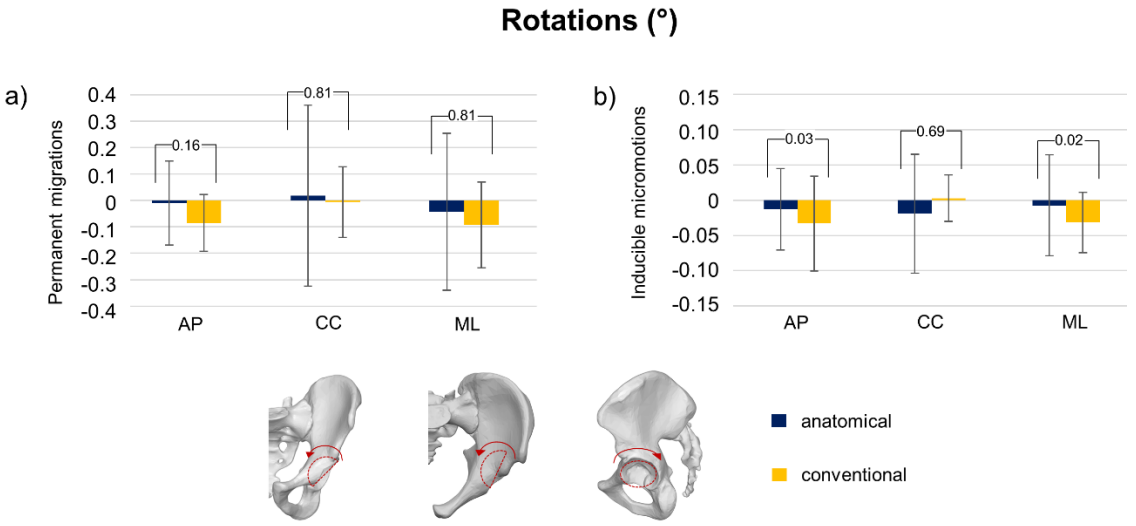


Fig. 5.4: Cup rotations when the largest load was applied to the anatomical and conventional implantations. The permanent migrations (a) and inducible micromotions (b) are presented as components of rotation about the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) axis. The three components of cup rotation are sketched together with a hemipelvis from the three views. The bars show the median and standard deviation of seven specimens. The *P*-value from the Wilcoxon signed-rank test is indicated for pairwise comparisons.

5.5 Discussion

The influence of cup medialization (or cup implantation depth) on initial stability of press-fit acetabular cups has not been clearly ascertained. Many Authors promoted an anatomical COR restoration in order to improve hip biomechanics and reduce long-term wear, but they mostly focused on the COR height [156]. Other Authors promoted cup medialization to improve long-term survival rates, but analyzed old-cemented implants affected with some sort of COR tridimensional displacement [160]. Thus, the optimal medial-lateral cup configuration has not been really assessed in cementless press-fit acetabular sockets: in particular, it is still unknown whether deeper acetabular implantation improves initial stability (and, thus, promotes a better bony ingrowth through minimization of micromotions).

Thus, an *in vitro* biomechanical study was performed on human hemipelvises. Press-fit acetabular cups were implanted, first aiming to restore the native COR (anatomical implantation), then reaming to the lamina (conventional technique). Thus, cup medialization was progressively increased (median value: 3.4±0.4 mm). The hypothesis was: cup medialization, and thus conventional reaming technique, improved primary cup

stability. However, the biomechanical results showed that anatomical and conventional implantations produced comparable implant motions. The permanent translations and rotations were similar for the two techniques, with no statistically significant difference. Only inducible rotations around the antero-posterior and the medio-lateral axes were significantly different. However, such rotations were so small in all cases (less than 0.04°, close to the intrinsic error of the measurement protocol[127]).

Literature about the relationship between cup medialization and implant stability is definitively limited. Only one study assessed the effect of reaming depth, bone defects and under-reaming in Sawbones foam block and bovine spongy bone specimens [23]. Adler *et al*. concluded that proper bone preparation (hemispherical cavity with no focal defects) and cup medialization (5 mm) improved cup stability. Adler *et al* proposed that cup medialization may have overcome dense subchondral bone and polar gaps, providing more stability [23]. O'Rourke *et al*. partially supported these suggestions in a non-focused paper, highlighting a non-significant correlation between polar gaps and intact acetabular depth (that is, minimal medialization) in a cohort of patient-specific finite element models [162].

These findings were not supported by the present study: cup medialization did not significantly improve cup stability. As a matter of fact, Adler *et al*. implanted the cups at three medial-lateral configurations, reaming 5 mm deeper every time [23]. However, Bonnin *et al*. implanted press-fit cups on 100 hips using conventional and anatomical techniques: the mean cup medialization was 3.2 mm±1.9, with higher values in males [160]. Thus, a medialization of 5 mm or more seems definitely too aggressive and not suitable for many pelvic morphologies. In fact, in the present study a medialization of 3.4 mm was provided by the conventional reaming technique with respect to the anatomical one. Moreover, the medial-lateral position of the cup plays a complex role in the whole hip biomechanics, impacting on offset and range of motion [163]. Aggressive medialization may definitively violate the acetabular offset and, in some cases, increasing femoral offset is not sufficient to compensate for the global loss of lateralization [157]. As a consequence, hip abductors lever arm may be compromised[160,164,165]. Moreover, recent literature highlighted that cup medialization and loss of offset were associated to increased wear of polyethylene liners and increased stresses at the bone-implant interface in press-fit sockets, overturning the classic perspective "more cup medialization-less loosening"

(based on cemented cups and very old implants)[166,160,167,159]. Conversely, anatomical reaming provides accurate COR reconstruction, adequate offset restoration and, as the present study highlighted, sufficient cup stability[160,156,157]. It also preserves bone stock, which is of paramount importance to date, considering that THAs are more and more common in younger patients and the rate of revisions is steadily increasing[160,168].

A limitation of this study is related to the two consecutive reaming techniques performed on the same acetabulum. The anatomical reaming and the subsequent biomechanical tests may have partially influenced the shape of the second acetabular cavity and the grip of the second cup implantation. Furthermore, the conventional reaming was performed using the last reamer used for peripheral acetabular preparation (without progressively increasing the reamer sizes from the beginning of the preparation). In this way, reaming is concentric with a medial-lateral vector (superior-inferior and anterior-posterior displacements do not take place) and cup medialization is the sole positioning variable. A single loading configuration was applied in our biomechanical tests, reducing the complexity of the forces acting in the acetabulum to a single resultant force. This simplification was demonstrated to be suitable to generate *in vitro* implant motions consistent with the clinical observations [147]. Our study had a limited sample size (N=7 hemipelvises); however, as the same specimen was used in testing of anatomical and conventional implantation, we could exploit pair-wise comparisons. A similar sample size is often used in *in vitro* implant stability tests[24,26]. The need to prevent bone damage (to allow testing each specimen in two implant conditions) forced us to limit the magnitude of the forces applied during the test. Therefore, absolute implant motions in real patients might be larger than those found in our tests. However, implant motions were analyzed in comparative terms, thus allowing to assess differences between anatomical and conventional implantation.

In summary, this study demonstrated that cup medialization did not improve initial stability of press-fit sockets. As previously highlighted in the literature, cup medialization may increase wear rate, stresses at the bone-implant interface, loss of bone stock and loss of offset, with significant effects on implant survival, biomechanics and stability[166,167,156,157,158]. Conversely, anatomical reaming closely restores the native COR and provides sufficient initial cup stability. Thus, cup medialization and conventional reaming technique should not be performed routinely, but mostly on individual basis

(when the acetabulum is still shallow and aspherical after peripheral reaming). Long-term studies comparing the two reaming techniques in the same patients (bilateral THAs) may provide additional decisive data about the clinical consequences of these two surgical approaches, in particular aseptic cup loosening, polyethylene wear and implant stability.

Chapter 6:

Primary stability of revision acetabular reconstructions using an innovative bone graft substitute: A comparative biomechanical study on cadaveric pelvises

From the manuscript:

Federico Morosato, M.Sc., Francesco Traina, MD., Ronja A. Schierjott, M.Sc., Georg Hettich, Ph.D., Thomas M. Grupp, Ph.D., Luca Cristofolini, Ph.D., Primary stability of revision acetabular reconstructions using an innovative bone graft substitute: A comparative biomechanical study on cadaveric pelvises (2020), *(submitted to The Journal of Arthroplasty)*

6.1 Abstract

Background: The main cause of hip implant failure is aseptic loosening of the acetabular component. Such failure is typically accompanied with defects in and around the acetabulum that must be restored during revision. Morselized bone graft represents the golden standard. Due to its limited availability, synthetic substitutes are adopted as an alternative material. We aimed to assess experimentally if a synthetic full-resorbable tri-calcium-phosphate-based bone graft substitute grants a good mechanical stability when used to treat severe contained defects, in comparison with morselized bone graft.

Methods: Each side of five cadaveric pelvises were alternatively treated with morselized bone graft or with graft substitute. The bone graft substitute consists of dense calcium-phosphate granules within a collagen matrix. The biomechanical test consisted of cyclic loading, where the load magnitude was increased until failure occurred. Digital Image Correlation (DIC) was used to measure the bone/implant motions in terms of permanent and inducible translations and rotations throughout the test.

Results: Both reconstruction types exhibited a settling trend during the first phase of the test. Failure occurred as bone fracture (i.e. no failure of the reconstruction material). The permanent translations when 2.2 Body-Weight was applied did not differ significantly between the two reconstruction technique (below 1.0 mm). Similarly, the inducible translations did not differ significantly (below 0.160 mm). Rotations differed qualitatively between reconstructions but had the same order of magnitude.
Conclusion: The proposed bone graft substitute granted adequate mechanical stability, providing a suitable synthetic alternative to morselized bone grafts to reconstruct severe contained acetabular defects.

Keywords: Revision hip surgery; severe contained acetabular defects; morselized bone graft; synthetic bone graft substitute; in vitro stability; biomechanical testing.

6.2 Introduction

Revision hip arthroplasty accounts for 10-15% of hip replacements performed worldwide every year[6,7,8,9,10]. The main cause of hip implant failure is aseptic loosening of the acetabular component, generally accompanied with bone loss, and the consequent generation of defects in and around the acetabulum[169]. To achieve a viable implant stability of the revision cup, the bone defects should be addressed before implantation of the prosthesis. Revision surgery in the presence of bone defects is challenging as material must be added to restore the bone loss. Impacted morselized bone grafts represent a popular solution, especially for contained defects [170,171,172]. However, due to the limited availability of human tissue, synthetic bone graft substitutes are adopted as alternative material[173]. In particular, calcium phosphate (CaP) -based materials such as hydroxyapatite (HA) or tri-calcium-phosphate (TCP) represent a reliable solution due to their availability, biocompatibility and osteoconductive properties[174].

One crucial point for such revision surgery is that sufficient primary stability must be provided to grant initial and long-term stability of the revision implant and of the augments when subjected to post-operative loading (which is cyclic by nature).

Arts *et al* investigated the effect of the size and of the washing of morselized bone graft, on the stability of acetabular reconstructions with segmental defects (AAOS Type III) [22]. Bolder *et al.* tested a different mix of bone grafts and TCP/HA granules, in combination

with acrylic bone cement in simplified geometry replicating the acetabulum, aiming to identify the combination that allows optimal cement penetration[29].

Other authors adopted a similar approach to study the mechanical stability of acetabula reconstructed with the impaction grafting technique and cemented cups[36,55,62]. To the Author's best knowledge in only one study morselized bone graft were compared with a resorbable synthetic CaP-based material adopted to reconstruct a cavitary defect (AOSS Type 2 defect) implemented in a cadaveric model[39].

Recently, a bone graft substitute made of tetrapods of TCP has been shown to grant sufficient load mechanical capacity in a very simplified bone defect model[175]. A previous study using a standardized bone defect geometry in acetabular foam models has shown the potential of bone graft substitutes made of molded bodies and a matrix material in granting implant stability[176].

Almost all the studies above concentrated on the combined use of resorbable materials and bone cement. So far, only one study, where an entire resorbable bone defect filler was tested was published. In the past, both segmental and contained defects have been addressed, but biomechanical analyses were mostly performed only on synthetic foam models of the acetabulum. To the author's knowledge cadaveric specimens were used in one *in vitro* study by Jacofsky et *al.*[39].

The aim of the present study was to assess if a resorbable CaP-based bone graft substitute can be used to treat severe contained central defects. In order to improve the handling properties of the bone graft substitute, the tetrapods of the previous studies[175] were embedded in a collagen matrix, resulting in a moldable CaP-putty. The hypothesis was that such a CaP-putty would provide similar primary stability as the conventional impaction bone grafting technique. Primary stability of the implant was measured and compared between the two techniques in terms of permanent migration and inducible micromotions using Digital Image Correlation (DIC).

6.3 Material and methods

Preparation of the specimens

Five pairs of fresh-frozen hemipelvises were obtained through ethically-approved donation programs (Table 1). This Study was authorized by the Bioethics Committee of the University of Bologna (Prot. 179610 of 7 December 2018). No information about donor's laterality was available. The bones were thawed at room temperature prior to testing. They were wrapped in cloths soaked with physiological saline solution when not in use. The soft tissues around the acetabulum and in correspondence of the anatomical landmarks were removed. Each hemipelvis was aligned in a reliable reference frame and potted in correspondence of the sacro-iliac joint in an aluminum pot with bone cement[82].

Tab. 6.1: List of specimens, including the donors' details, and the size of the implanted cups. The last column reports the difference between the two reconstruction materials for the acetabular defects.

Donor	Cause of death	Sex	Age (years)	Height (cm)	Body weight (kg)	BMI (kg/m^2)	Side	Primary cup size (mm)	Revision cup size (mm)	Reconstruction material
#1	Sepsis	Female	83	164	63	23	L	56	58	Bone graft
							R	56	58	CaP putty
#2	Respiratory paralysis	Male	70	175	79	26	L	52	54	Bone graft
							R	54	56	CaP putty
#3	Unknown	Male	74	176	78	25	L	48	50	CaP putty
							R	48	50	Bone graft
#4	Coronary thrombosis	Male	71	187	92	26	L	60	62	Bone graft
							R	62	64	CaP putty
#5	Cardiac arrhythmia	Male	61	181	96	29	L	56	58	Bone graft
							R	54	56	CaP putty
Median		**-**	**71**	**176**	**79**	**26**	**-**	**55**	**56.6**	**5 vs 5**
SD		**-**	**7.9**	**8.5**	**13.2**	**2.2**	**-**	**4.5**	**4.3**	

In order to replicate consistent defects in each hemipelvis, a standardized protocol for defect implementation, based on statistical shape modelling and quantitative defect analysis, was adopted[176,177]. Critical, contained defects were replicated representing mostly medial defect with rim damage of approximately one third of the circumference, located at the inferior-posterior area of the rim (Fig. 6.1). To enhance consistency, each

defect was scaled on anatomical features of the native acetabulum: the thickness of the acetabular roof, the thickness of the anterior column and the thickness of the posterior wall.

Each hemipelvis and its contralateral side were randomly selected to be treated CaP-putty or with morselized bone graft (Fig. 6.1). Acetabular reconstruction was performed by an experienced surgeon. The morselized bone chips were prepared from a proximal femoral epiphysis using a rongeur in order to achieve a medium diameter of the bone chips of about 8mm. The bone chips were impacted into the bone defect gently hammering with a dedicated hemispherical impactor. The bone chips were added since the contained defect was fulfilled and even with the acetabular surface of the acetabulum. The same procedure was done with the CaP-putty

The CaP-putty consisted of TCP-tetrapods within a collagen matrix. The putty should provide a loadable, osteoconductive, and osteoactive putty to reconstruct large acetabular bone defects. A recent study showed the load capacity and the osteoconductive properties of the tetrapods without collagen[175]. To improve the handling properties and to include a kind of osteoactive stimulus, the tetrapods were embedded within a collagen matrix in a weight ratio of 95% tetrapods and 5% collagen. A tetrapods/collagen slurry was prepared and filled in cavities with a length of 5 cm. Using lyophilization, bars of tetrapod/collagen bars were created. In contact with water, the bars become moldable and were used in the present study to fill the defect in form of a CaP-putty. The collagen matrix collapses when the putty is impacted and the tetrapods have contact to each other. After resorption of the collagen, an osteoconductive scaffold for bone ingrowth is expected to remain.

Commercial cups (Plasmafit PLUS 7, Aesculap, Tuttlingen, Germany) were press fitted into the acetabular cavity and two anchoring screws were inserted medially to enhance stability (Fig. 6.1). Whenever possible, the same cup size was implanted in the contralateral hemipelvises (in three cases a discrepancy of one size was required to accommodate for the asymmetry of the same donor).

To allow the DIC software to correlate, a high-contrast black-on-white speckle pattern was applied on the specimen surface.

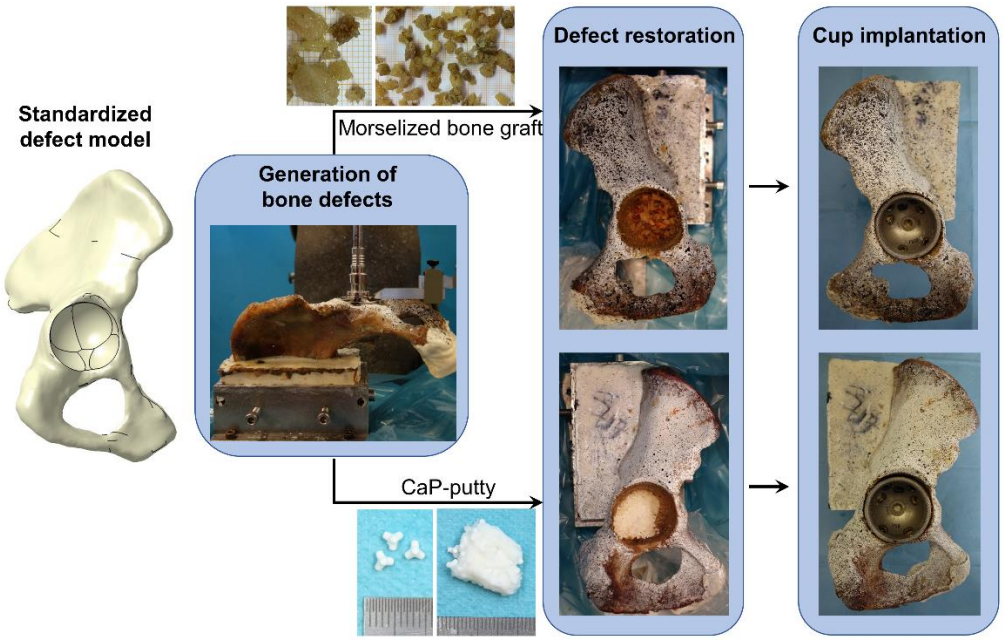


Fig. 6.1: The standardized acetabular defect was implemented based on the statistical shape model developed in Schierjott *et al.*[177]. The hemipelvis was machined in consecutive steps using different commercial surgical reamers, with reproducible defects scaled according to the specimen-specific dimensions. Each hemipelvis and its contralateral side were alternatively reconstructed with morselized bone graft or CaP-based material. Commercial cups were press-fit in the acetabular cavity and two anchoring screws were used.

Biomechanical testing

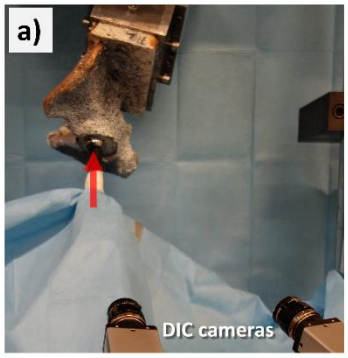
A validated protocol was used for the biomechanical testing[127]. Walking was selected among the recommended activities for post-op rehabilitation. In particular, the direction of the peak force measured *in vivo* during level-walking was extracted from open datasets [77] and a custom mechanical setup was produced so as to apply the force in the selected direction during the biomechanical test. A servo-hydraulic testing machine was used to load the specimens. The test consisted of 50-cycles load packages with increasing amplitude. The first load package (up to 1 BW) served as pre-conditioning. Then, the biomechanical test was extended, increasing the load until visible specimen failure. (Fig. 6.2).

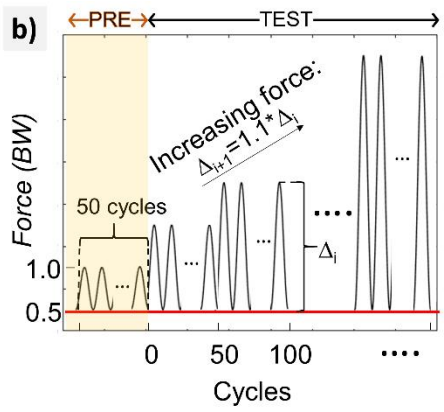
Measurement of implant motion and strains

A commercial DIC system (Q400, Dantec Dynamics, Denmark) was used to measure the motions of implant and bone. Two cameras (5 MegaPixels, 2440 ×2050 pixels, 8-bit) equipped with high-quality metrology-standard 17 mm lenses (Xenoplan, Schneider-

Kreuznach, Bad Kreuznach, Germany) were used to obtain 3D measurements. The cameras were positioned so as to frame the implant and the superior aspect of the acetabulum (Fig. 6.2).

In order to compute the bone/implant motions (translations and rotations along/about cranio-caudal, antero-posterior and medio-lateral axes), the DIC-measured displacements were post-processed through a dedicated script in Matlab (2017 Edition, MathWorks, Natick, MA)[127]. In particular the permanent migration (i.e. the migration accumulated cycle after cycle), and the inducible micromotion (i.e. the recoverable motion between load peak and valley) were analyzed.





Package	Last cycle	Preload (BW)	Amplitude (BW)	Peak (BW)
PRE	50	0.50	0.50	1.00
1	100	0.50	0.55	1.05
2	150	0.50	0.61	1.11
3	200	0.50	0.67	1.17
4	250	0.50	0.74	1.24
5	300	0.50	0.81	1.31
6	350	0.50	0.89	1.39
7	400	0.50	0.98	1.48
8	450	0.50	1.08	1.58
9	500	0.50	1.19	1.69
10	550	0.50	1.31	1.81
11	600	0.50	1.44	1.94
12	650	0.50	1.58	2.08
13	700	0.50	1.74	2.24
14	750	0.50	1.91	2.41
15	800	0.50	2.10	2.60
16	850	0.50	2.31	2.81
17	900	0.50	2.54	3.04

Fig. 6.2: (a) The specimen was aligned in the testing frame so as to apply a force (arrow) in a direction that replicated level walking. The cameras of the DIC system were placed so as to frame both the cup and the surrounding bone. (b) Load cycles of increasing magnitude were applied: each load packages consisted of 50 cycles; each package was 10% larger than the previous one; the force was scaled on the patient body weight (BW). The first load package (50 cycles 1.00 BW) was used for pre-conditioning before the actual test.

Statistical analysis

In order to exclude outliers, the Peirce's criterion was applied. To assess if the effects on implant motions deriving from the two bone reconstruction materials were statistically different, a Wilcoxon signed-rank test was performed at each load level. The level of significance was p=0.05 for all analysis. All stats were performed with Matlab.

6.4 Results

The digital image correlation system was able to track the motions between the cup and the bone throughout the biomechanical tests.

The specimens failed at different load magnitudes, between 2.4 and 5.0 BW. Failure was not due to the implant, but to fracture of the posterior column. In order to compare the effect of the bone reconstruction material on implant stability, the results will be presented up to 3 BW, which corresponds to the magnitude of the peak load measured in the hip during walk [77]. This force magnitude was reached before bone fracture in all specimens but one: in this case all the load packages preceding fracture could be compared to the other specimens.

The permanent migration steadily increased throughout the test as load increased (Fig. 6.3). Migration showed a visible settling trend from the beginning to the end of each single load package (of 50 cycles each) at low forces, whereas migrations kept growing during each of the last load packages (higher forces). At 2.2 BW (all specimens reached this level), the resultant permanent migration for the specimens with bone graft were 0.57 mm (median; range: 0.12-2.26 mm) and with CaP-putty were 0.95 mm (median; range: 0.33-2.67 mm). At 3.0 BW the permanent migration (for 4 specimens that reached 3 BW) with bone graft were 0.84 mm (median; range: 0.26-2.67 mm) and with CaP-putty were 1.39 mm (median; range: 0.69-3.43 mm). The difference of migrations between the two groups was statistically not-significant at all load levels (Wilcoxon signed rank sum test, p=0.06-1.0 for the different load packages).

The inducible micromotions had a more irregular trend (Fig. 6.3). They were generally constant or slightly decreasing within the same load package for lower loads. When the implant started migrating, also the micromotions fluctuated within the same load package. Large inducible micromotions were typically followed by larger permanent migrations. At 2.2 BW the inducible micromotions for the specimens with bone graft were 0.11 mm (median; range: 0.06-0.21 mm) and with CaP-putty were 0.16 mm (median; range: 0.05-0.32 mm). At 3.0 BW the micromotions (for 4 specimens that reached 3 BW) with bone graft were 0.15 mm (median; range: 0.15-0.43 mm) and with CaP-putty were 0.24 mm (median; range: 0.05-0.53 mm). The difference of inducible micromotions between the

two groups was statistically not-significant at all load levels (Wilcoxon signed rank sum test, p=0.06-1.0 for the different load packages).

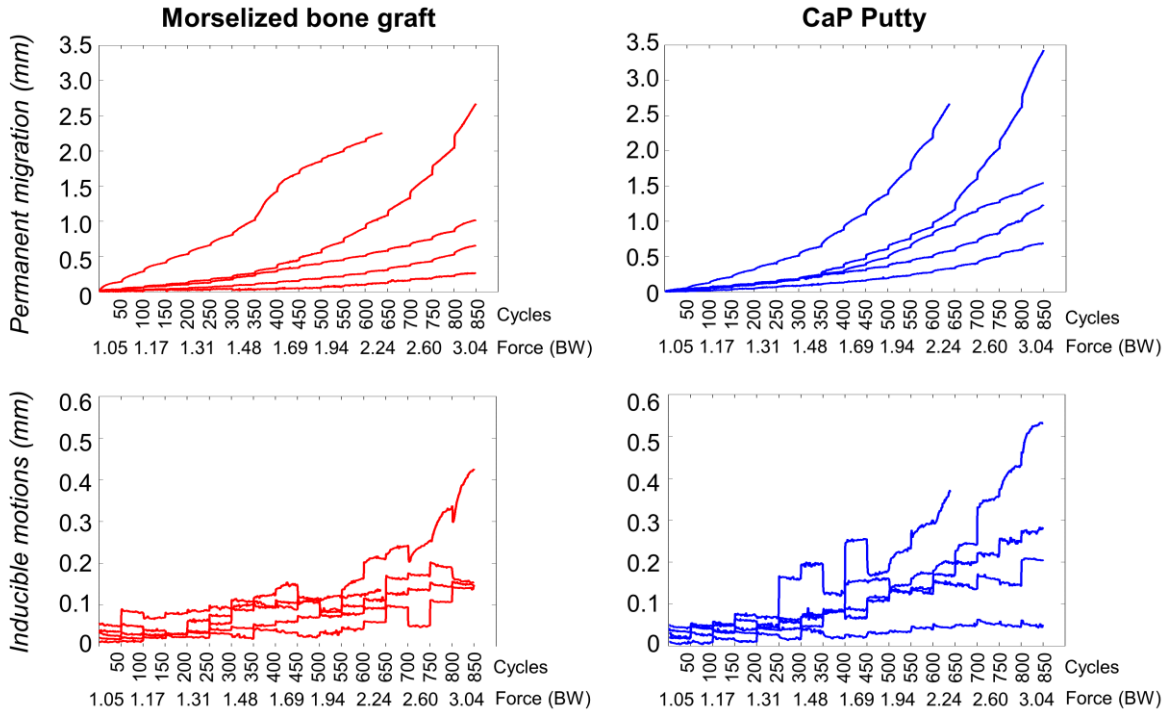


Fig. 6.3: The resultant permanent migration and the resultant inducible micromotions measured during each test are shown for the morselized bone graft (left, n=5 specimens) and CaP putty (right, n=5 contralateral specimens).

Looking at the single motion direction, the largest permanent translation occurred along the medio-lateral axis for both the reconstruction techniques (Fig. 6.4, 6.5). At 3.0 BW, the permanent translations along the cranio-caudal and the antero-posterior axes were on average respectively 31 % and 47 % of the translation along the medio-lateral axis for reconstructions with bone graft and 24 % and 87 % for reconstructions with CaP-putty. The largest component of permanent rotation was about the antero-posterior axis (i.e. change of inclination).

The inducible translations and rotations had differences between components similar to those observed for the permanent ones, but varied significantly between specimens and during the test (Fig. 6.4, 6.5).

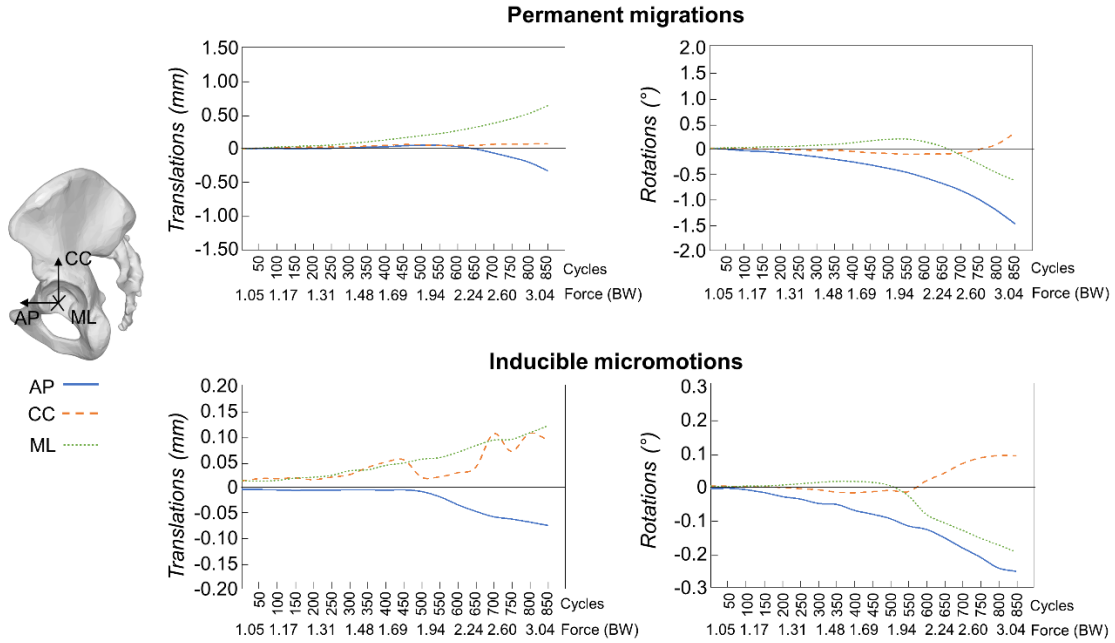


Fig. 6.4: Morselized bone graft: The permanent migrations and inducible micromotions throughout the test are presented as the median trend of the specimens. For the translations, the components along the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) directions are reported. The rotations are reported in terms of individual components about the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) axis.

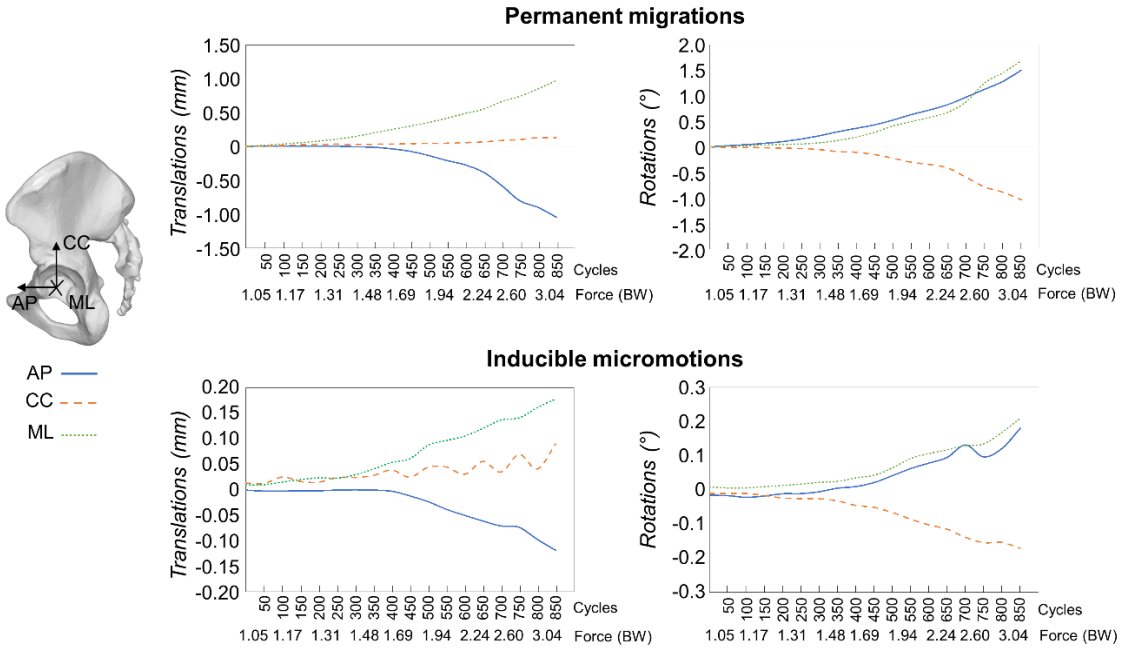


Fig. 6.5: CaP putty: The permanent migrations and inducible micromotions throughout the test are presented as the median trend of the specimens. For the translations, the components along the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) directions are reported. The rotations are reported in terms of individual components about the antero-posterior (AP), cranio-caudal (CC) and medio-lateral (ML) axis.

6.5 Discussion

The aim of the present study was to assess if a resorbable CaP based bone graft substitute in form of a putty can provide adequate stability in case of revision surgery with severe contained central acetabular defects. The CaP putty was compared with impaction bone grafting, assumed as the golden standard.

Digital Image correlation was used to assess the bone/implant motions when a cyclic load of increasing magnitude was applied. In all tests, specimen failure was reached when the bone fractured. In fact, all specimen fractured in the posterior column at different load magnitudes. In none of the specimens failure was due to excessive deformation or failure of the reconstruction material. The resultant permanent migration at 2.2 BW were below 1.0 mm for both reconstruction techniques, thus below the clinical threshold associated to late implant loosening[19]. At the same load magnitude, inducible micromotions were below 160 micrometers for both techniques, close to the value generally assumed to grant osteointegration in real bone[18]. It must be noticed that the inducible migration measured is not just interface micromotion, but is partly due to the deformation of the graft material. Therefore, the actual interface micromotions were definitely lower. Furthermore, the permanent migrations exhibited a settling trend within each load package up to 2.2 BW (i.e. most of the permanent migration occurred within the first cycles of each load package as the applied force was increased). Also, the inducible micromotions were generally constant or slightly decreasing within the same load package, confirming the tendency to settle within each load package.

Both the permanent migrations and the inducible micromotions motions in the specimens reconstructed with CaP putty were generally larger than with bone graft. However, this difference was not statistically significant. The average measured cup migration found in past studies had the same order of magnitude of the one of the present study, but larger cup motions were associated with defects reconstructed with morselized bone graft [22,29,55,62]. Such results differ from results of other studies that investigated the acetabular stability in case of reconstructed defects. Such difference may be related to the type of defect, the reconstruction techniques and the test methods adopted to assess the acetabular stability. In most studies central, cavitary, contained defects were implemented (similar to AAOS Type 2 defects), while in our study the defect also significantly involved the

posterior column. For this reason, even if the largest migration was measured along the medio-lateral axis (i.e. in line with all of the studies mentioned above), a large cup migration was also measured in the direction of the posterior column. In most studies cups were cemented within a layer of reconstruction material (whether bone graft or synthetic), used to fill the cavity, while in the present study, cups were press-fitted, and two screws were added to enhance the stability. Only Jacofsky *et al*. applied a loading direction comparable with the one adopted in the present study, simulating a level walking. In that study, they compared the effect on acetabular stability of defect filling with bone graft and with a bioresorbable calcium-phosphate injectable material, applied in cadaveric hemipelvises. The accumulated cup migration was larger with bone graft but the difference with the synthetic material was lower than 20 micrometers at the end of the test. Moreover, the settlement trend was in line with our study, i.e. the bone graft stabilized progressively during the test, while, the synthetic material used in that study showed an increasing rate of migration[39].

Some limitations of the present work must be mentioned. The sample size was limited due to specimen availability. However, as the test was devised to compare two reconstruction techniques, paired specimens were adopted; thus, providing a reliable comparison. Moreover, the number of the specimen is comparable with the sample size of other biomechanical analyses related to implant stability[39,24,26]. The load applied was limited to a single direction, reducing the complexity of forces and moments acting in the acetabulum. Such approach, already adopted by most authors, has been proved to induce cup motions comparable with the clinical observation while granting a good robustness and reliability of the results (i.e. minimizing the sources of experimental error [127]). Moreover, as paired tests were performed, the effect of the loading configuration on the acetabular stability is reduced if compared with the effect of the reconstruction material. The current study focused on contained defects. Thus, results may be different in case of different types of acetabular defects (i.e. segmental or uncontained defects) or defects with a different distribution of bone loss in general.

Overall, the study demonstrated that the resorbable CaP putty bone graft substitute proposed in the present study granted a mechanical stability comparable with the golden standard technique (morselized bone graft) when applied in the acetabulum with severe, contained defects. The material was tested up to 3 BW representing a critical peak load

for patient undergoing revision surgery. For lower forces (more reasonable for revision patients) the difference from the morselized bone graft was minimal. In both cases the clinical thresholds related to implant failure (i.e. 1 mm for the permanent migration and 150 micrometers for the elastic motions) was not exceeded. Such results confirmed the good load capacity of the proposed material[175], overcoming the lack of mechanical stability that calcium-based materials generally have. In conclusion, this study has shown very promising biomechanical properties of the newly developed CaP putty, when applied to severe contained defects, with remarkable advantages in terms of cost, availability, conservation and body-rejection.

Chapter 7: Conclusions

The overall project provided interesting and useful results for studying the hip biomechanics, focusing on the acetabular side of the joint. In particular:

- A robust reference frame suitable for the human hemipelvis was defined. Due to its good reliability and simple *in vitro* implementation, it may constitute a good starting point for researchers working on hip biomechanical testing. Moreover, as it is based on anatomical landmarks belonging only to one side of the human pelvis, it simplifies the specimen preparation while keeping the operator variability very low;
- A reliable method to assess the hip acetabular stability through Digital Image Correlation (DIC) was developed. Due to the high accuracy of the DIC measurements in combination with the proposed method, small bone/implant motions (order of the μm) can be detected with high accuracy and precision (better than 16 μm), distinguishing between permanent and elastic motions. Moreover, thanks to a good optimization process for strain measurements, also periacetabular strains can be measured with high accuracy and precision (better than 150 με);
- It was shown that the simulated motor tasks affected the direction of the cup migration and the magnitude of the periacetabular strains. Both walking and standing up generated cup migrations comparable with cup migrations observed clinically. Therefore, it could be useful to include both the motor tasks in experimental analysis of cup stability. Periacetabular strains increased significantly when unstable implants were tested, especially in case of standing up. Such result may provide indications for the post-operative patient activities (e.g activities to avoid during the rehabilitation therapy).
- It was shown that cup medialization did not significantly affect the cup stability of press-fit implants. This result contributes in the clinical debate about the influence of cup medialization on acetabular stability, suggesting that, as it is associated with a number of negative effects such as an increased wear rate and loss of bone stock, it should not be performed routinely.
- It was shown that the innovative bone substitute presented in the study provided a hip cup stability similar to the stability provided by human bone graft, when

adopted to restore severe contained acetabular defects. This result proves that synthetic alternatives for defect filling may have a significant impact in the clinical practise: in fact, in addition to the already proved advantages in terms of cost, availability, conservation and body-rejection, they can also provide good mechanical stability, if properly engineered.

To conclude, the project provided a significant contribute in better understanding the hip biomechanics and in answering some clinical questioned problems. Reliable methodological basis were set in order to support researchers and clinicians working on hip biomechanics. For the first time DIC was used to investigate biomechanical problems about cup stability, providing the scientific community of new methods and (hopefully) incentives in using such measurement technique to explore human biomechanics. Different clinical critical problems were investigated, and the results may provide surgeons of new suggestions for the clinical decision-making process.

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