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**Original Article: Long-Term Hip Loading in Unilateral Total Hip Replacement Patients is no
Different between Limbs or Compared to Healthy Controls at Similar Walking Speeds**

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26 **Abstract**

27 Variation in hip joint contact forces directly influences the performance of total hip replacements
28 (THRs). Measurement and calculation of contact forces in THR patients has been limited by small
29 sample sizes, wide variation in patient and surgical factors, and short-term follow-up. This study
30 hypothesised that, at long-term follow-up, unilateral THR patients have similar calculated hip
31 contact forces compared to controls walking at similar (self-selected) speeds and, in contrast, THR
32 patients walking at slower (self-selected) speeds have reduced hip contact forces. It was further
33 hypothesised that there is no difference in calculated hip contact forces between operated and non-
34 operated limbs at long-term follow-up for both faster and slower patients. Gait analysis data for
35 THR patients walking at faster (walking speed: 1.29 ± 0.12 m/s; $n = 11$) and slower (walking speed:
36 0.72 ± 0.09 m/s; $n = 11$) speeds were used. Healthy subjects constituted the control group (walking
37 speed: 1.36 ± 0.12 m/s; $n = 10$). Hip contact forces were calculated using static optimisation. There
38 was no significant difference ($p>0.31$) in hip contact forces between faster and control groups.
39 Conversely, force was reduced at heel strike by 19% ($p=0.002$), toe-off by 31% ($p<0.001$) and
40 increased at mid-stance by 15% ($p=0.02$) for the slower group compared to controls. There were no
41 differences between operated and non-operated limbs for the slower group or the faster group,
42 suggesting good biomechanical recovery at long-term follow-up. Loading, at different walking
43 speeds, presented here can improve the relevance of preclinical testing methods.

44 **1 Introduction**

45 Total hip replacement (THR) is a well-established and largely successful orthopaedic procedure,
46 which is primarily employed to treat end-stage osteoarthritis (UK National Joint Registry, 2017).
47 The UK National Joint Registry reports 13-year revision rates of less than 7% for the majority of
48 bearing types (UK National Joint Registry, 2017). Although hip joint contact forces (HCFs) are
49 related to both short-term (e.g. implant micromotion) and long-term THR failure mechanisms (e.g.
50 peri-prosthetic bone remodelling) (Sumner, 2015), direct measurement has only been possible in
51 small samples of disparate patients using instrumented implants (Bergmann et al., 2001; Davy et al.,
52 1988; Rydell, 1966). Musculoskeletal models have been used to calculate HCFs from three
53 dimensional motion capture data and ground reaction forces, with good agreement to instrumented
54 implant measurements (Heller et al., 2001; Modenese et al., 2011; Modenese and Phillips, 2012;
55 Stansfield et al., 2003). Nevertheless, musculoskeletal modelling of HCFs in THR patients has been
56 limited by small sample sizes, short-term follow-up, and wide variation in patient, surgical, and
57 implant factors (Foucher et al., 2009; Li et al., 2014; Stansfield and Nicol, 2002; Wesseling et al.,
58 2016a).

59 Recently, musculoskeletal modelling of healthy subjects reported that walking speed has a
60 considerable impact on predicted HCFs (Giarmatzis et al., 2017, 2015). Unfortunately, studies
61 reporting HCFs in THR patients have not controlled for walking speed or have been confined to a
62 few patients at short-term follow-up (Bergmann et al., 1993; Heller et al., 2001; Li et al., 2014;
63 Modenese and Phillips, 2012; Stansfield et al., 2003; Wesseling et al., 2016a). It is unclear whether
64 differences observed (e.g. lower HCFs compared to controls) in THR patients relative to healthy
65 subjects are due to walking speed, variable or short-term follow-up, or other surgical outcomes.

66 Hip moments in THR patients have been reported to be significantly altered at both short-term
67 (Beaulieu et al., 2010) and long-term follow-up (Bennett et al., 2017) compared to controls. At
68 short-term follow-up, differences in HCFs for THR patients compared to controls have also been
69 found across a range of surgical approaches, even with similar walking speeds (Wesseling et al.,

2016b). When comparing between limbs, differences have been observed in hip moments between operated and contralateral limbs (Foucher and Wimmer, 2012). However, Li et al. (2014) found no difference in HCFs between limbs 12 months after unilateral THR. To the authors' knowledge, no long-term study has been conducted comparing THR patients' HCFs at different speeds to controls and between limbs.

This study hypothesised that, at long-term follow-up, unilateral THR patients have similar calculated HCFs compared to controls walking at similar (self-selected) speeds and, in contrast, THR patients walking at slower (self-selected) speeds have reduced HCFs. It was further hypothesised that there is no difference in calculated HCFs between operated and non-operated limbs at long-term follow-up for both faster and slower patients.

80 **2 Methods**

81 **2.1 Patient and control data**

82 All patients received unilateral THRs in Musgrave Park Hospital (Belfast, UK) under the senior
83 author (DEB) using a posterior approach with the same cemented implants (Orthogenesis custom
84 X-press femoral implant and Elite acetabular implant, DePuy International, Leeds, UK). All had a
85 28 mm femoral head articulating with an ultra-high molecular weight polyethylene acetabular
86 implant.

87 Three dimensional gait analysis was undertaken using retroreflective markers placed according
88 to the Helen Hayes marker set (Kadaba et al., 1990). At least three walking trials were performed
89 along a central walkway (8–10m length) and a single representative trial was used for analysis. All
90 patients and control subjects walked bare foot. Data was captured at 120 Hz using a six-camera
91 Vicon 612 system and patients walked at self-selected speed. Patients were stratified by walking
92 speed and the 11 slowest and 11 fastest patients (out of a total of 134 patients) with sufficient force
93 plate data for operated and non-operated limbs were used for musculoskeletal analysis. Force plate
94 data was collected at 120 Hz using two force plates (AMTI, Watertown, MA) and assessed visually
95 using Mokka (Version 0.6, BioMechanical Toolkit) (Barre and Armand, 2014). Force plates were
96 fully concealed and integrated into the floor covering. To avoid targeting, patients were not told of
97 their position and instructed to walk at their normal walking speed. Patients were studied 10 years
98 post-operatively: follow-up ranged from 9.72 to 10.41 years for slower patients and 9.13 to 10.18
99 years for the faster cohort. Three-dimensional gait data from 10 healthy elderly controls was also
100 used for musculoskeletal analysis. Controls and THR groups' age ranges and body mass index
101 (BMI) are presented in Table 1. Ethical approval was obtained from the local ethics committee
102 (Queen's University Belfast, Faculty of Medicine, Research Ethics Committee, Reference number:
103 253/02).

104 **2.2 Musculoskeletal modelling**

105 A lower extremity model, “gait2392”, with 12 segments, 23 degrees of freedom and Hill-type
106 models of 92 muscle-tendon compartments was used to analyse gait with a standard static
107 optimisation workflow in OpenSim 3.3 (Stanford University, CA, USA) (Delp et al., 2007, 1990).
108 Lumbar extension, lumbar bending, lumbar rotation, metatarsophalangeal and subtalar joints were
109 fixed in anatomical neutral positions for all analyses. A zero-lag low-pass filter with a cut-off
110 frequency of 6 Hz was applied to ground reaction forces and kinematics (Mantoan et al., 2015).
111 Isotropic scaling of the generic model segments was performed based on markers placed on bony
112 landmarks of the subject with the exception of the pelvis, where the laboratory-measured distance
113 between the left and right anterior superior iliac spines was used (Figure 1).

114 Inverse kinematics and inverse dynamics were performed to calculate joint angles and moments
115 respectively. Static optimisation was executed to estimate the muscle activations and forces. The
116 objective function for static optimisation minimised the sum of the muscle activations (defined as
117 the ratio of predicted force relative to maximum isometric force for the muscle) squared based on a
118 study showing that this criterion produces realistic HCFs and muscle activation patterns relative to
119 instrumented implant and EMG data (Modenese et al., 2011). In accordance with OpenSim best
120 practice, reserve actuators were added to the joint between the pelvis and the ground to account for
121 dynamic inconsistencies caused by errors in the model estimations of the subject’s inertial
122 parameters and geometry as well as marker placement/tracking inaccuracies. Force-length-velocity
123 relationships were not used for the muscle models in this study as they have been shown not to
124 affect the calculation of HCFs for level walking (Anderson and Pandy, 2001). Finally, a joint
125 reaction analysis was performed in OpenSim in order to calculate the resultant hip force, i.e. HCF.
126 All HCFs were subsequently normalised to body weight (BW) and the moments were divided by
127 body mass in kilograms (Nm/kg).

128 **2.3 Data analysis and statistics**

129 The start and end of the gait cycle were identified and 100-point splines were fitted to the HCFs and
130 hip moments for both sides in MATLAB (2015b, TheMathWorks, Inc., MA, USA). These points
131 were used to create ensemble average curves for the control, slower patient, and faster patient
132 groups. Ensembles curves were also created for comparison between operated and non-operated
133 limbs in both the faster and slower patient groups. Peaks in HCF at heel strike, mid-stance, and toe-
134 off were identified for quantitative statistical analysis. These points within the gait cycle were also
135 used to compare hip adduction moments, while hip flexion moments were compared using
136 maximum and minimum values of a complete gait cycle and hip rotation moment was compared
137 using only the maximum value. Differences between HCFs and moments for operated and non-
138 operated peaks were tested using the paired Wilcoxon Signed Rank-Sum Test as the data were not
139 normally distributed. Control subjects were compared (by hip kinematics, HCFs and hip moments)
140 to the speed-stratified groups with a Wilcoxon Rank-Sum Test using a Bonferroni correction for
141 multiple comparisons. In cases where a Bonferroni correction was used, the p-value has been
142 multiplied by the number of comparisons so that the interpretation is the same for all data, i.e.
143 $p < 0.05$ is significant. All statistical analysis was performed using R (Version 3.4.0) (R Core Team,
144 2017).

145 **3 Results**

146 Maximum hip extension was significantly ($p < 0.001$) reduced in slower THR patients compared to
147 controls (Figure 2; Table 2). Similarly, hip adduction range was significantly lower ($p < 0.01$) for
148 both THR groups (i.e. slower and faster) compared to controls (Figure 2; Table 2). Overall, hip
149 moments tended to be reduced in the THR groups compared with the control group (Figure 2; Table
150 3). In particular, the slower group had lower peak extension ($p < 0.001$; Figure 2) and internal
151 rotation moments ($p = 0.002$; Figure 2) when compared to control subjects; this trend was matched

152 by the faster patients for extension ($p=0.002$; Figure 2) and internal rotation moments ($p=0.03$;
153 Figure 2). The abduction moment showed a similar trend to HCFs, i.e. distinct double peak for
154 faster and control groups while slower patients showed a higher mid-stance moment ($p<0.05$),
155 similar in magnitude to the heel-strike and toe-off peaks. In terms of magnitude, the faster THR
156 patients' moments were more comparable to the control group than the slower THR group.

157 Ensemble averaged HCFs of faster THR patients and control subjects showed a distinct double
158 peak profile whereas slower THR patients exhibited lower HCFs and a plateau during stance phase
159 (Figure 3). There were significant differences in HCFs between slower THR subjects and control
160 subjects at heel-strike ($p=0.002$), mid-stance ($p=0.02$) and toe-off ($p<0.001$) (Table 4 and Figure 3).
161 Conversely, there was no statistical difference ($p>0.31$) between these forces in faster THR patients
162 compared to controls (Figure 3). There were no significant differences between operated and non-
163 operated limb HCFs at heel-strike, mid-stance, or toe-off ($p>0.10$) for either the faster or slower
164 patient groups (Figure 4).

165 **4 Discussion**

166 The first hypothesis of this investigation was that calculated HCFs in THR patients at long-term
167 follow-up are comparable to healthy control subjects at similar walking speeds and HCFs of slower
168 patients are significantly reduced. We also hypothesised that HCFs of operated and non-operated
169 limbs in THR patients were not significantly different at long-term follow-up. The results supported
170 both hypotheses. Slower patients showed a less dynamic HCF profile whereas both faster and
171 control groups showed increased contact forces at the beginning and end of stance phase and lower
172 contact force at mid-stance. There was no difference in hip contact forces throughout the gait cycle
173 between operated and non-operated limbs in either the faster or slower groups.

174 Hip contact forces from this study compare well with experimentally measured HCFs (via
175 instrumented implants) at similar walking speeds. For example, instrumented implant measurements
176 by Bergmann et al. (1993) at a walking speed of 0.83 m/s (the closest comparison for our slower

177 group speed of 0.72 ± 0.09 m/s) averaged 3.5 BW for peak HCF compared to 2.98 BW in our study.
178 Predicted HCFs, using a similar musculoskeletal modelling approach, for elderly healthy subjects
179 walking at 0.83 m/s also show good agreement with our findings at low walking speeds, peaking at
180 3.3 BW (Giarmatzis et al., 2017). At a walking speed of 1.38 m/s, and for elderly female patients,
181 Giarmatzis et al. (2017) estimated a mean hip joint loading at the first peak of 4.3 BW and 4.6 BW
182 at the second peak, while Weinhandl et al. (2017) predicted peaks of 3.39 ± 0.45 BW and $4.61 \pm$
183 0.55 BW for a cohort of five male and five female young, healthy subjects walking at 1.34 ± 0.07
184 m/s. The values presented here are similar at 3.5 ± 0.6 BW and 4.5 ± 0.9 BW.

185 In the studies described above, excluding Weinhandl et al. (2017), subject speed was controlled
186 using a treadmill rather than being self-selected. Similar HCFs have been predicted for disparate
187 cohorts when walking speed was matched, e.g. Giarmatzis et al. (2017) showed very similar force
188 profiles between young and old groups at matched walking speeds between 0.83 m/s and 1.94 m/s.
189 Walking speed in our study was self-selected and patients were not tested on a treadmill. Walking
190 speed is related to physical and mental function (Peel et al., 2013) with faster patients generally
191 expected to have better function. Consequently, our study is likely capturing the best functioning
192 THR patients in the faster cohort and the worst in the slower group.

193 A previous study (Li et al., 2014) using different musculoskeletal modelling methodology
194 showed similar trends but altered magnitudes: Li et al. (2014) presented HCFs for a relatively
195 young control group (average age: 44.97 years) walking at 1.44 m/s (1.39 –1.50 m/s) and found a
196 considerably lower mean toe-off peak of 3.67 BW compared to controls in this study and the
197 publications by Giarmatzis et al. (2015) and Weinhandl et al. (2017) on healthy subjects. These
198 differences are most likely due to the methodological approaches, with Li et al. (2014) opting for
199 the Anybody software (AnyBody Technology, Aalborg, Denmark) and model while the other
200 studies, including the current, use OpenSim with the “gait2392” model. These two modelling
201 approaches have shown altered muscle force estimations in a comparative study (Trinler et al.,

202 2017), which can be a result of separate scaling and mathematical optimisation processes in each
203 software.

204 With regard to comparisons between operated and non-operated limbs, the findings in this
205 investigation are in agreement with previous works at short-term follow-up (Beaulieu et al., 2010;
206 Benedetti et al., 2010; Li et al., 2015, 2014). The close matching of hip contact force profiles
207 between operated and non-operated limbs suggests good biomechanical recovery at long-term
208 follow-up. The absence of difference in HCFs between operated and non-operated limbs for both
209 faster and slower patients suggests symmetrical biomechanical recovery is achieved, which is
210 independent of walking speed. Foucher and Wimmer (2012) report an increased abduction moment
211 in the non-operated hip preoperatively compared to speed-matched controls, with no improvement
212 up to 1 year following THR. In contrast, we found no significant difference in hip abduction
213 moment between faster patients compared to normal subjects and significantly lower hip internal
214 rotation and extension moments, which may be due to the longer period of recovery (Figure 2).

215 Strengths of this study include control of possible confounding surgical and patient factors. In
216 addition, many previous works have assessed HCFs shortly after surgery when patients have
217 variable levels of recovery whereas we report HCFs at long-term follow-up (Bergmann et al., 2001;
218 Heller et al., 2001; Li et al., 2014; Stansfield et al., 2003; Stansfield and Nicol, 2002).

219 Notwithstanding these strengths, there were several important potential limitations to this
220 study. Firstly, gait kinematics, kinetics, and walking speed have been shown to be age-related
221 (Bennett et al., 2017, 2008), and there was an age difference between the slower THR and control
222 groups in this study. However, Giarmatzis et al. (2017) have shown that walking speed difference
223 would be expected to influence kinetics independent of age. Secondly, patients were stratified by
224 walking speed from a larger dataset (Bennett et al., 2008), meaning patients walking at mid-range
225 speeds were not included. In our opinion, assessing the extremes of walking speed has the
226 advantage of establishing more useful ranges for preclinical testing design that are relevant to the
227 increasing volume of THR procedures being performed (UK National Joint Registry, 2017). Lastly,

228 while the sample sizes in this study are based on previous works with similar aims (Foucher et al.,
229 2009; Li et al., 2014; Stansfield and Nicol, 2002; Wesseling et al., 2016a), future studies involving
230 larger sample sizes would likely add to the findings presented here.

231 Limitations in the modelling aspects of this investigation include isotropic scaling of a generic
232 musculoskeletal model based on the location of gait markers, as used here and in similar studies
233 (Giarmatzis et al., 2015; Weinhandl et al., 2017). This may be susceptible to misplacing the joint
234 centres and is particularly pertinent since previous validation studies have used CT and X-ray
235 derived joint centres (Modenese et al., 2011; Stansfield et al., 2003). This has increased relevance in
236 THR patients as the location of the hip joint centre is often shifted following THR surgery (Bonnin
237 et al., 2012). Previous studies suggest that the location of the joint centre may be improved through
238 the use of medical imaging (Kainz et al., 2017; Lenaerts et al., 2009) or a functional method
239 (Leardini et al., 1999). Lenaerts et al. (2009) compared CT measurements to a linear scaled generic
240 model, finding an anterior and proximal shift of the hip joint centre location of 30mm and 20mm
241 respectively; this did not cause a significant effect on the magnitude of HCFs but did influence the
242 orientation of the force. Future investigations examining the accuracy of hip joint centre location in
243 THR patients would help in the interpretation of this work.

244 The findings of this study have important implications for preclinical testing of THR implants
245 and patient recovery. Firstly, there were considerable differences in HCFs (both in force profile
246 shape and magnitude of loading) between slower and faster THR patients suggesting preclinical
247 simulation studies should include this loading variability. Secondly, this study shows that self-
248 selected walking speed is associated with contact force in the hip joint and should therefore
249 influence study design when comparing THR patients to controls. Thirdly, HCFs (and moments,
250 Appendix 1) are similar between operated and non-operated limbs at long-term follow-up
251 suggesting patients have good biomechanical recovery.

252 In conclusion, the hypothesis that there is no difference between healthy control subject HCFs
253 and THR patient HCFs at similar walking speeds was supported by this study. We also showed

254 there to be large differences between slower THR patients and both control and faster groups. The
255 difference between a faster and slower THR patient, in terms of HCF, is substantial and is relevant
256 to both computational and lab-based preclinical testing methods and many biomechanical failure
257 mechanisms of THR. In addition, we found contact forces to be no different between the operated
258 and non-operated hips at both faster and slower walking speeds. This equalisation may be indicative
259 of the longer recovery period studied here.

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264 **Conflict of interest**

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267

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362

1 **Table 1: Subject details for walking speed stratified groups; data is presented as mean $\pm$ standard deviation**

Group	Number of Subjects	Walking Speed (m/s)	Age (Years)	BMI (kg/m ²)	Years to Review	Gender (M:F)
Slower	11	0.72 $\pm$ 0.09	74.18 $\pm$ 7.21	29.81 $\pm$ 4.99	10.00 $\pm$ 0.20	8:3
Faster	11	1.29 $\pm$ 0.12	70.56 $\pm$ 4.88	25.34 $\pm$ 3.51	9.76 $\pm$ 0.30	6:5
Control	10	1.36 $\pm$ 0.12	64.00 $\pm$ 3.60	26.22 $\pm$ 3.01	N/A	6:4

2

3

1 **Table 2: Kinematics comparison between slower THR, faster THR and controls. Data is presented as mean $\pm$ standard deviation.**

2 *****=p<0.001, **=p<0.01 and *=p<0.05 for differences between THR groups and control group only.**

	Maximum hip extension (°)	Hip Adduction range (°)	Hip rotation range (°)
Slower	-2.8 $\pm$ 11.1***	8.0 $\pm$ 4.1***	18.6 $\pm$ 6.8
Faster	-15.5 $\pm$ 7.5	10.9 $\pm$ 3.3**	23.0 $\pm$ 6.7
Control	-19.4 $\pm$ 6.1	13.8 $\pm$ 2.3	20.6 $\pm$ 6.4

3

4

1 **Table 3: Moments comparison between slower THR, faster THR and controls. Data is presented as mean $\pm$ standard deviation.**

2 *****=p<0.001, **=p<0.01 and *=p<0.05 for differences between THR groups and control group only.**

	Max. flexion moment (Nm/kg)	Max. extension moment (Nm/Kg)	HS abduction moment (Nm/kg)	MS abduction moment (Nm/kg)	TO abduction moment (Nm/kg)	Maximum internal rotation moment (Nm/kg)
Slower	0.33 $\pm$ 0.11***	-0.63 $\pm$ 0.26	-0.64 $\pm$ 0.18*	-0.60 $\pm$ 0.15**	-0.68 $\pm$ 0.16	0.11 $\pm$ 0.07**
Faster	0.59 $\pm$ 0.10**	-0.82 $\pm$ 0.20	-0.76 $\pm$ 0.18	-0.50 $\pm$ 0.15	-0.74 $\pm$ 0.16	0.13 $\pm$ 0.07*
Control	0.76 $\pm$ 0.18	-0.83 $\pm$ 0.25	-0.82 $\pm$ 0.18	-0.44 $\pm$ 0.14	-0.76 $\pm$ 0.16	0.17 $\pm$ 0.07

3

4

1 **Table 4: Hip contact forces for all groups; data is presented as mean $\pm$ standard deviation. “slower” and “faster” groups are an average**
2 **of the operated and non-operated hips. ***= $p<0.001$, **= $p<0.01$ and *= $p<0.05$ for differences between THR groups and control group**
3 **only for slower, faster and control groups. No statistical differences were evident between operated and non-operated hips.**

Group	Heel-strike force (BW)	Mid-stance force (BW)	Toe-off force (BW)
Slower	$2.98 \pm 0.67^{**}$	$2.70 \pm 0.63^{*}$	$3.18 \pm 0.71^{***}$
Faster	3.43 ± 0.62	2.35 ± 0.57	4.49 ± 0.94
Control	3.79 ± 0.71	2.17 ± 0.54	4.92 ± 0.93
Slower – Operated	3.08 ± 0.62	2.73 ± 0.68	3.24 ± 0.74
Slower – Non-Operated	2.89 ± 0.68	2.67 ± 0.55	3.13 ± 0.68
Faster – Operated	3.22 ± 0.62	2.25 ± 0.58	4.07 ± 0.64
Faster – Non-Operated	3.63 ± 0.53	2.44 ± 0.53	4.91 ± 0.96

4

1

2 **Figure 1:** Overview of the workflow for musculoskeletal modelling. In the objective function J , n is

3 the number of muscles in the model, F_i is the force of the i_{th} muscle and $F_{isomax,i}$ is the maximum

4 isometric force of the muscle.

5

Kinematics

Moments

Figure 2: Inverse kinematics and dynamics results for control (solid line), slower THR (dotted), and faster THR (dashed). See Table 2 (kinematics) and Table 3 (moments) for detailed numerical data and statistical testing results.

Figure 3: Hip joint contact forces over one gait cycle for slower and faster THR patients compared to elderly control subjects. There were no statistical differences between the control and faster THR groups at any of the three points analysed. Asterisks denote difference (***= $p < 0.001$, **= $p < 0.01$ and *= $p < 0.05$) between controls and speed stratified groups only and are followed by 'slow' for difference between slower and control subjects and 'fast' for differences between faster and control subjects.

*=p<0.05, **=p<0.01, ***=p<0.001, ns = not significant

Figure 4: Comparison of operated and non-operated HCFs for slower (A) and faster (B) groups.

'ns' refers to differences that were not significant.

2
3 **Figure 5:** Comparison of moments between operated and non-operated limbs. Maximum hip
4 extension moment in faster THR patients was the only peak with a statistical difference ($p<0.05$)
5 between operated and non-operated hips.