ORIGINAL ARTICLE

Use of the Pixel Value Ratio Following Intramedullary Limb Lengthening: Uncomplicated Full Weight-bearing at Lower Threshold Values

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Abstract

Aims: The pixel value ratio (PVR) can be used to assess regenerate consolidation after lengthening and guide advice for full weight-bearing (FWB). This study aimed to analyse the PVR in adults having femoral lengthening, the time to FWB and compare findings with the reported values in the literature.

Materials and methods: A retrospective database review identified 100 eligible patients who underwent lengthening using the PRECICE nail (68 antegrade and 32 retrograde). The PVR was calculated in each cortex on plain radiographs at every visit. The ratio between the regenerate and an average from the adjacent normal bone was calculated and plotted against the clinical decision to allow FWB.

Results: Eighty-seven patients (58 men and 29 women) were assessed; eleven had bilateral lengthening and two patients underwent lengthening twice. The median age was 30.5 years. The underlying cause of shortening was post-traumatic in 46%, with the remaining due to a wide variety of causes, including congenital 16%, syndromic 12% and other causes. The median lengthening achieved was 45 mm, at a median of 57.5 days. The PVR increased with each visit (p <0.0001). FWB was allowed at a median of 42 days after the last day of lengthening, with PVR values of 0.83, 0.84, 0.93 and 0.84 for the anterior, posterior, medial and lateral cortex noted, respectively (average 0.85). There were no implant failures, shortening or regenerate fractures. No differences were detected between antegrade and retrograde nails or with lengthening greater or less than 45 mm. One surgeon allowed earlier FWB at median 31 days with no nail failures.

Conclusion: PVR is a valuable tool that quantifies regenerate maturity and provides objectivity in deciding when to allow FWB after intramedullary lengthening with the PRECICE nail. FWB was permitted at an earlier time point, corresponding with lower PVR values than have been reported in the literature and with no mechanical failure or regenerate deformation.

Keywords: Intramedullary lengthening, Intramedullary limb-lengthening system, Pixel value ratio, Regenerate, Weight-bearing.

Strategies in Trauma and Limb Reconstruction (2022): 10.5005/jp-journals-10080-1542

Introduction

Limb reconstruction through the use of the tension stress effect on the growth and regeneration of tissue, as described by Ilizarov, has evolved to treat a huge variety of conditions.[1,2] The circular external fixator was the cornerstone of this method. The success achieved was tempered by the cumbersome nature of the frame, soft tissue tethering and irritation from pins and wires, joint stiffness, as well as psychological and social implications.[3,4] Many techniques have been used to decrease treatment duration and to reduce potential complications.[2,4] Intramedullary lengthening devices can abolish the need for external fixators altogether with good outcomes.[5–8]

Timing of the removal of an external fixator remains difficult. Early removal risks damage to regenerate integrity, producing a deformity or fracture. Late removal leads to an increase of joint, pin site and soft tissue complications. The study of optimal regenerate consolidation has been undertaken in several studies through utilising plain radiographs, computed tomography, dual-energy X-ray absorptiometry scan and ultrasound.[9]

The pixel value ratio (PVR) is a ratio comparing the pixel value of the regenerate to the adjacent normal bone on a digital radiograph. This has been shown to be a reliable assessment of regenerate bone healing in both external fixation and intramedullary lengthening techniques.[10–17]

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How to cite this article: Elsheikh AA, Wright J, Stoddart MT, *et al.* Use of the Pixel Value Ratio Following Intramedullary Limb Lengthening: Uncomplicated Full Weight-bearing at Lower Threshold Values. Strategies Trauma Limb Reconstr 2022;17(1):14–18.

Source of support: Nil

Conflict of interest: None

The decision to allow full weight-bearing (FWB) with an intramedullary lengthening nail remains subjective. The PRECICE intramedullary limb-lengthening system (ILLS, NuVasive Inc., San Diego, California) comprises a magnetic actuator, gearbox and piston within a titanium sheath. Several studies have confirmed excellent results.[6–8,18–20] There are, however, risks of nail bending and failure which can occur if regenerate consolidation is inadequate and too much weight is allowed through the limb.[21] The manufacturer advises a limitation in weight-bearing of 20–30 kg until an adequate regenerate consolidation, often described as formation of three out of four cortices.[19,22]

Two recent studies have highlighted the value of using the PVR in assessing regenerate consolidation to determine the time to permit FWB.[23,24] The aim of this study is to measure the PVR at the point when FWB is allowed in a consecutive group of patients who have undergone femoral lengthening with the PRECICE nail and to see if the early weight-bearing protocol as used occurred at a lower PVR.

Materials and Methods

A retrospective radiological analysis was performed on a consecutive group of adult patients who underwent femoral lengthening using the PRECICE ILLS between September 2012 and November 2019 at a single centre. Approval was granted by the institutional research and development committee (R&D registration number: SE21.11). Patients with less than 12 months of follow-up and those with an oblique osteotomy, which distorted the calculation in some views, were excluded. There were 100 femoral lengthening (53 right side and 47 left side) in 87 patients (58 men and 29 women) eligible for review. The median age at surgery was 30.5 years [IQR (interquartile range) 22 years, range 18–68].

Eleven patients had bilateral sequential lengthening and two patients underwent lengthening of the same segment twice. All procedures were performed by two senior limb reconstruction surgeons (surgeon A performed 55 procedures, and surgeon B performed 45). There were 68 antegrade and 32 retrograde lengthening undertaken. The indications and underlying pathologies were variable; 46% were acquired shortening, 16% congenital, 12% syndromic and 26% had various causes of limb length discrepancy.

All patients had a standard application of the PRECICE nail, either antegrade or retrograde, with a distraction rate of 0.33 mm three times a day.[19] The PVR was measured on the radiograph from the first outpatient attendance after the last day of lengthening and on every subsequent visit. The decision to allow FWB was made by the senior consultants based on clinical criteria without the influence of PVR; both surgeons applied different regimens. Surgeon A permitted patients to increase weight through the lengthened limb gradually with 25% in the first week, 50% in the second, 75% in the third and finally FWB through the limb at 4 weeks after completion of lengthening. After a further week, anteroposterior and lateral plain radiographs were taken, and if adequate regenerate consolidation in the distraction site was confirmed, as determined by the evidence of increased bone density in three out of four cortices, then FWB was continued. If the regenerate was thought to be inadequate, then partial weight-bearing was reinstituted. Surgeon B instructed patients to remain partial weight-bearing, placing no more than 20 kg through the limb. FWB was permitted after subsequent radiographs confirmed adequate regenerate consolidation as above. FWB was permitted for the most at the second outpatient visit after completion of lengthening (57%), while in 37% of patients it was allowed at the third visit. In 6% of cases, FWB was delayed to a later visit (fourth or fifth). The time interval to FWB was calculated from the end of lengthening.

Radiographic images were assessed using the McKesson Enterprise Medical Imaging PACS, release 12.3 (2017) system. PVR calculations were recorded for the anterior, posterior, medial and lateral areas by utilising the “region of interest (ROI)” modality. Anterior and posterior values were collected from the lateral radiographic view whilst the medial and lateral values were collected from anteroposterior views. This particular imaging package offers an oval, not rectangular, outline of ROI. Values of the ROI were measured carefully to ensure that only the bone density was recorded (cortex and medulla) without the inclusion of the nail which would have distorted the readings (Fig. 1).

The PACS system that was used has a proportional measurement of the pixel value; increased density produces a bigger number (Fig. 1). The PVR was calculated in a similar way to earlier reports:[10,17]

$$\frac{\text{Regenerate pixel value}}{[\text{proximal pixel value} + \text{distal pixel value}] \times 0.5}$$

A PVR of one represents a regenerate that is of equivalent density to that of the adjacent bone. A PVR of less than one indicates a lower radiographic density of the consolidating regenerate than the adjacent bone.

Statistical analysis was undertaken with data entered into the Statistical Program for Social Science, the IBM SPSS version 24.0 (IBM Co., Armonk, New York, USA). Median and interquartile

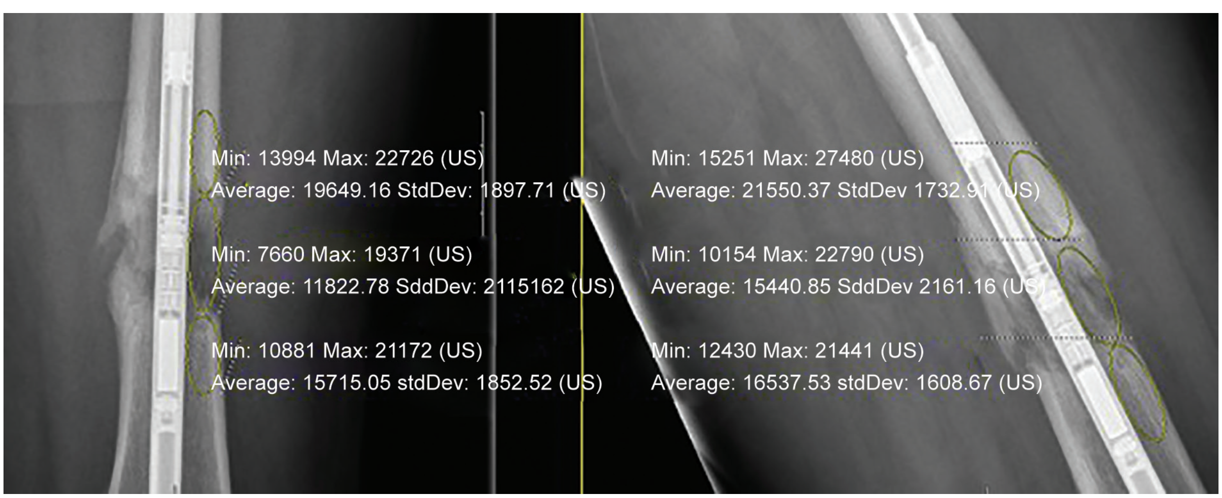

Fig. 1: PVR measurement of the regenerate ROI, proximal and distal normal bone segments

range was used to express the spread of data. Analytic statistics in the form of Chi-square for test correction, the Mann–Whitney test for comparing two groups and the Wilcoxon test for assessing the change between different readings of every individual. The Kruskal–Wallis test was used to detect any difference between more than two groups. The variables included sex, antegrade vs retrograde and amount of lengthening achieved.

Results

The median lengthening achieved was 45 mm (IQR 30, range 15–80 mm), at a median of 57.5 days (IQR 37, range 20–146 days). FWB was allowed at a median of 42 days (6 weeks) after the last lengthening day (IQR 39, range 21–210 days). When calculated from the day of surgery, this interval had a median of 105 days (15.5 weeks) (IQR 39, range 60–309 days). No mechanical failure of the device was recorded in the cohort of patients.

At the time of FWB, the regenerate-segment PVR had a median value of 0.83, 0.84, 0.93 and 0.84 for the anterior, posterior, medial, and lateral cortices, respectively. The overall median PVR was 0.85 (Table 1).

There was a statistically significant correlation between the surgeon and the time to FWB ($p = 0.013$); surgeon A tended to allow FWB at a median of 31.5 days (IQR 18, range 21–128), compared to surgeon B, who preferred FWB at a later date at a median of 55.5 days (IQR 40, range 28–210). However, there was no statistically significant difference in the PVR values at the time of FWB between the patients of surgeon A compared to surgeon B.

When the PVR value was calculated at serial outpatient attendances, there was a statistically significant increase in density compared to the previous visit (Table 2).

The age of patients in the antegrade nail group had a median of 28 years (IQR 22, range 18–68) and was significantly lower than those in the retrograde group (median 38 years, IQR 24, range 18–66) ($p = 0.041$); otherwise, there were no differences in patient demographics or lengthening achieved. Following retrograde nail lengthening, a slightly higher PVR value was recorded (in anterior, posterior and medial cortices) at FWB than the antegrade group, yet this difference was not statistically significant (Table 3).

Table 1: PVR values at the time of FWB

	Anterior	*Posterior*	*Medial*	*Lateral*	*Average*
Median	0.83	0.84	0.93	0.84	0.85
IQR	0.21	0.21	0.11	0.15	0.14
Minimum	0.42	0.47	0.61	0.39	0.54
Maximum	1.11	1.11	1.13	1.26	1.11

Table 2: PVR values at consecutive outpatient visits

	Visit 1 (end of lengthening)	*Visit 2*	*Visit 3*
Median of average PVR	0.761	0.841	0.907
Wilcoxon test *p* value	Visit 1 vs Visit 2 <0.000		
		Visit 2 vs Visit 3 <0.000	

Table 3: PVR values—antegrade vs retrograde nails

Ante/Retro	*Anterior*	*Posterior*	*Medial*	*Lateral*	*Average*
Ante	0.83	0.84	0.92	0.84	0.85
Retro	0.86	0.87	0.94	0.84	0.87
Whole cohort	0.83	0.84	0.93	0.84	0.85
p value	0.181	0.172	0.156	0.953	0.226

This cohort was divided into two groups using length gained; the median of the entire cohort was 45 mm and this was used as a division to create the two groups. Group I (<45 mm lengthening) comprised 54 cases (37 antegrade and 17 retrograde nails) and allowed FWB at a median of 46 days (IQR 40, range 21–140). Group II (>45 mm lengthening) had 46 cases (31 antegrade and 15 retrograde nails) and allowed FWB at a median of 42 days (IQR 36, range 21–210). There was no statistically significant difference between the two groups in the time to FWB after the end of distraction ($p = 0.181$). Additionally, the PVR values at FWB were also not statistically different ($p = 0.342$).

A review of the aetiology of shortening confirmed that patients with congenital and syndromic conditions were operated on at a younger age ($p < 0.000$), required more lengthening ($p < 0.000$) and took a long time to achieve the target length ($p = 0.039$). The syndromic group had the shortest time to FWB at a median of 28 days ($p = 0.008$), although this is the smallest group with only 12 lengthening episodes in 7 patients. In the congenital group, the PVR was significantly lower in the posterior cortex, with a median value of 0.75 compared to the whole cohort median of 0.84 ($p = 0.047$). No other differences were detected from the remaining cortices.

Discussion

The PRECICE intramedullary lengthening nail is proven to be a valuable tool in femoral lengthening.[19,20] The weight-bearing status remains an issue with the manufacturer's recommendation of no more than 20 kg of weight through the limb until adequate regenerate consolidation has occurred so as to reduce the risk of implant breakage and deformity.[22] In this retrospective review of a patient cohort who had completed femoral lengthening, we assessed the time when FWB was allowed by calculating the PVR and confirmed an earlier time to FWB, as compared to recent reports, is possible with no implant complications.[23,24]

The use of PVR was studied in limb reconstruction scenarios originally to quantify the regenerate quality and provide an objective assessment to time external fixator removal. Shim et al. studied the serial changes of the PVR during femoral (26 patients) and tibial (22 patients) lengthening with an external fixator. They concluded that PVR could be used reliably as a measure of regenerate maturation and aid in the timing of frame removal.[10]

Other methods of measuring regenerate maturation include bone mineral density (BMD), measured by a DEXA scan.[9] The correlation of PVR to BMD has been confirmed by Hazra et al., who compared the values of 70 tibial regenerate columns at the time of external fixation removal.[11] Song et al. further reported a linear correlation between the two methods in their study of 40 tibial lengthening using the Ilizarov frame.[14]

Early frame removal when performing the lengthening over nail (LON) technique is not without implant complications. Metalwork failure, screw breakage and nail bending have been reported.[25–27] Zhao et al. analysed 34 patients who underwent tibial LON, incorporating PVR to guide weight-bearing status. Partial weight-bearing was allowed once the PVR reached one in two cortices and full weight-bearing once the PVR reached one in three cortices. They reported no mechanical failures or refractures. Incidentally, this value was achieved in different cortices between

7 and 14 months and is much higher than the PVR level reported in this study to allow FWB.[12]

Two recent studies have correlated the PVR at the time for FWB after lengthening with the PRECICE ILLS. Bafor et al. analysed a cohort of 42 adults and paediatric patients, with a mean femoral lengthening of 36 mm.[23] Bone union was reported at 17 weeks (8–28) from the date of surgery. The PVR values at that time were measured at 0.93, 0.92, 0.96 and 0.93 in the anterior, posterior, medial and lateral cortices, respectively. Vulcano et al. analysed 32 patients, including both adults and paediatric patients, who had an antegrade PRECICE femoral lengthening of a mean of 41 mm.[24] They reported that bone union and FWB were achieved at 8.5 weeks (4–18). Due to soft tissue shadow overlying the proximal part of the regenerate, they only relied on the distal area for evaluation. The PVR was found to be 0.92, 0.98, 0.89 and 0.84 in the anterior, posterior, medial and lateral cortices. In comparison, this study reports lower PVR values at the time of FWB and an interval, whether from the day of surgery (105 days) or the completion of lengthening (42 days), which was shorter than that published from these other studies.

With traditional external fixation methods, the formation of three cortices has been described as a threshold for fixator removal.[28] In comparison, the formation of two cortices within the regenerate has been suggested in hybrid (combined internal and external) fixation, with the nail acting as a third cortex.[12] This is the premise for early weight-bearing out of frame with hybrid techniques using more rigid fixation.[4,25–27] The lengthened nail itself, whilst of limited strength, will contribute to the stability of the nail–regenerate construct. We believe that this acts in a similar (load sharing) manner to a steel bar contained within reinforced concrete, such that greater loads can be tolerated than by either component alone. This would also include resistance to axial loading through the locking bolts.

Despite starting with similar PVR values at the first visit post-lengthening, there was a trend for higher PVR values and a narrower IQR with surgeon A at the second and third visits; it appeared that PVR reaches a higher level faster to allow FWB through allowing a gradual increase in weight over 1 month. Given that there were no failures in our series we cannot define the lowest PVR threshold for weight-bearing, and it could be hypothesised that weight-bearing may be able to start even earlier.

At present, this is the largest series of patients undergoing surgery with a lengthening intramedullary nail in which the PVR has been assessed. We have only evaluated an adult cohort of patients, and the results may differ in paediatric and adolescent groups, in whom faster healing times have been reported.[19,20,28] The previous reports did not differentiate the outcome between adults and paediatrics, or antegrade vs retrograde nails.[23,24] We did not detect any difference in PVR between antegrade and retrograde nails in this study. We accept other limitations, as a retrospective analysis of the PVR matched to a known outcome. The PVR value was not able to be recorded as an absolute number. Despite measuring the median of the average PVR as 0.85, there was a wide range from 0.54 to 1.11. Therefore, it would be difficult to conclude and recommend a safe value to use. A PVR range between 0.71 and 0.99 could be considered, which contained the middle half of recorded values (IQR 0.14). However, further prospective studies are required.

Conclusion

The use of PVR is a valuable tool by allowing a standardised assessment of regenerate consolidation on X-ray. It may quantify regenerate strength and allow greater confidence when deciding to allow full weight-bearing after intramedullary lengthening with the PRECICE ILLS. This study has reported FWB at an earlier time point with smaller PVR values in comparison to the literature with no mechanical failure or regenerate deformation.

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