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Case Report

Photobiomodulation Therapy (PBMT) is Feasible and Acceptable in Pre-conditioning and Post-operative Recovery of Patients after Total Knee arthroplasty (TKA): A Clinical Case Series

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Abstract

Photobiomodulation therapy (PBMT) for minimal to moderate Kellgren and Lawrence grade knee osteoarthritis has significant evidence for effectiveness. The effect of PBMT in severe grades of osteoarthritis is less clear; and no studies have investigated the effect of PBMT before and after knee replacement surgery. This small study (n=4) aimed to understand the potential feasibility of undertaking a future randomised controlled clinical trial of a self-administered, home-based light patch system before and after total knee arthroplasty (TKA) The PBM device (450nm (6.75 mW/cm^2) and 640nm (2.25 mW/cm^2); 33kHz frequency, 4.5 J/cm^2 radiant exposure) was self-applied by patients daily for 30 minutes for one week before, and 3 times in the week following hospital discharge after TKA. We measured

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numeric pain ratings, physical function and patient-reported outcomes at baseline one week prior to surgery, the day prior to surgery, at Day 4 after surgery, and at 1, 2, 4 and 6 weeks after hospital discharge. The study protocol and methods were found to be feasible and acceptable to participants. No pain was reported by any participants at 6-week follow-up. Functional measures of timed-up-and-go and 30 second chair stands test demonstrated marked improvement over the study period. No patients were requiring opioid analgesia at 6-week follow-up. Limitations included lack of gender diversity, the small number of participants and absence of information about post-hospital discharge opioid analgesic requirements from control group. The results provide confidence in progressing this research in an adequately powered, placebo-controlled, randomised clinical trial.

Keywords
Photobiomodulation; pre-conditioning; post-operative pain; post-operative function; total knee arthroplasty

1. Introduction

Photobiomodulation (PBM) therapy (PBMT) has received significant attention in recent years for its effectiveness in treating symptoms of knee osteoarthritis (KOA). A recent systematic review [1] showed that low-level laser PBM at 4 to 8 J per treatment spot in wavelengths between 785–860 nm, and PBM at 1 to 3 J with 904 nm wavelength when compared with placebo, significantly reduced pain and disability by the end of the treatment period and in short- to medium-term follow-up. Many studies combine PBM with exercise (in different combinations) demonstrating the compounding effect of PBM [2]. Where noted, the mean Kellgren and Lawrence criterion in 13 studies of PBM therapy (PBMT) in KOA [1] was 2.37 (highest grade = 4: severe OA [3]) thus it would appear that the benefit of PBM and exercise has been established mostly in mild to moderate grades of KOA. In recent published study protocols [4, 5] the authors propose to combine PBM with other treatment methods, and these studies will be conducted in participants with Kellgren and Lawrence grades 3 or less.

In severe grades of KOA (Kellgren and Lawrence grade 4), total knee replacement surgery is often undertaken to correct misalignment of the knee joint and reduce the pain and disability from degenerative tissue changes. We have noted previously [6] (a) that total knee arthroplasty (TKA) is an effective method of alleviating pain and restoring function of the knee joint; and (b) the increase in numbers of TKA as populations age. For example, the Australian Institute of Health and Welfare reported a 38% rise in the rate of total knee replacements for KOA from 2005-06 to 2017-18 [7]. In 2020, more than 62,000 new knee replacement procedures (including total and partial knee replacements and joint revisions) were added to the Australian Orthopaedic Association National Joint Replacement Registry [8]. Due to the COVID-19 pandemic, the number was fewer compared to previous years for the first time since the Registry started, most likely due to the temporary cessation of elective surgery in Australia during various stages of the pandemic.

Although the outcomes of TKA are generally good, approximately 1 in 5 patients who have had knee replacement surgery, are dissatisfied with the result, many due to ongoing pain [9]. For

example, Khan et al. [10]) noted that "Pooled data from registries worldwide identifies that the most common indication for revision surgery is aseptic loosening (29.8%), followed by infection (14.8%) and pain (9.5%)". In Australia, the five highest reasons for knee joint revision surgery were infection (26.4%), prosthetic loosening (22.7%), instability (9.5%), patella-femoral pain (8.4%) and pain (8.1%) [8].

As pain remains a significant problem in many patients who undergo knee replacement surgery, the risk remains of opioid ingestion by patients for prolonged periods post-operatively, and resultant misuse or abuse of opioids; and the possible need for and expense of joint revision surgery. PBM as peri-operative therapy is only beginning to be explored as an alternative to pharmacological therapies (e.g., Nunes et al [11]; Kazemikhoo et al [12]). To our knowledge, only one study has demonstrated the post-operative benefit of PBM therapy in reducing acute pain and inflammation in patients after total hip arthroplasty [13].

This paper reports the results of a feasibility study in which we proposed the use of a novel 3D-printed light patch for use in pre-operative conditioning of the quadriceps muscles and lymph vessels at the groin and popliteal fossa, and for post-operative management of pain in TKA [6]. The aims were to understand factors related to participant acceptability and tolerance of the intervention, to note any adverse effects, and determine if post-operative pain, functional recovery, and opioid requirements could be influenced.

2. Materials and Methods

The study was a prospective, open-label, clinical feasibility study with no randomization or placebo. The materials and methods have been described elsewhere [6].

Participants between 60 and 87 years of age awaiting planned unilateral TKA were recruited from the waitlist of a single Orthopaedic Surgeon in a tertiary teaching hospital at a major Australian city. Patients were excluded if they had a pre-existing pain syndrome such as peripheral neuropathy; a history of stroke, or of previous surgery or severe trauma to the knee to be operated on; severe back pain and arthritis significantly affecting mobility or referring pain to the operated leg; significant cognitive dysfunction that would prevent ability to consent to participation in the study; or a medical diagnosis of significant mental ill health which could impact upon the post-operative recovery period. All participants gave fully informed, written consent.

Self-administered, pre-conditioning treatment with the light patches (CareWear Corp, USA; Carewear Firefly Controller and Carewear Firefly Lamps; https://www.carewear.net/) occurred daily in the participants' homes for 1 week prior to surgery, and every second day for 1 week after discharge from hospital. The light patches (consisting of approximately 3000 light emitting microdiodes over a medium patch area of 34cm^2; and 5000 light emitting microdiodes over a large patch area of 56.7cm^2) emitted combined wavelengths of 450nm (6.75 mW/cm^2) and 640nm (2.25 mW/cm^2) at 33kHz frequency, and 4.5 J/cm^2 radiant exposure for 30 minutes treatment time at each application site. Seven light patches [6] were applied at the groin and popliteal fossa, over the quadriceps muscles (Figure 1), above and below the knee and at the medial knee joint line pre-operatively. To accommodate the transparent wound dressing after hospital discharge, six patches were applied at the groin and popliteal fossa, over the upper quadriceps muscles, and at the medial and lateral knee joint line post-operatively. All participants were educated at the first home visit on use and care of the devices and provided with written instructions. Telephone

follow-up of participants during the treatment phases was maintained to ensure that participants were applying the devices appropriately, and application of the devices was checked before the post-operative treatment phase commenced.

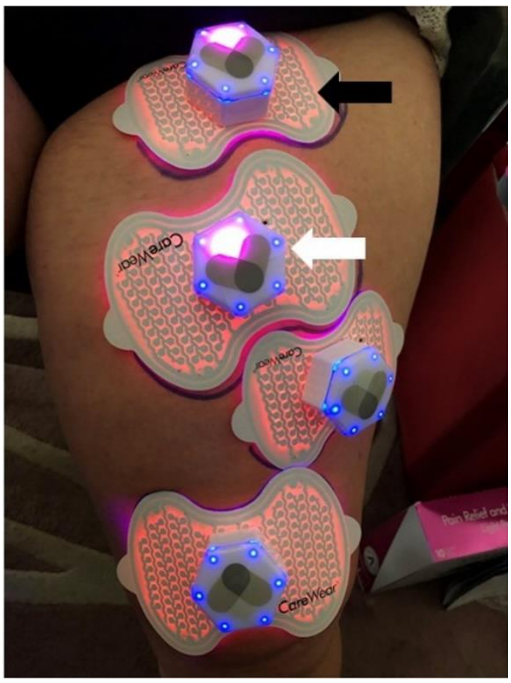

Figure 1 Indicative image of light patch application to front of thigh. White arrow points to Firefly Controller; Black arrow points to a medium size light patch.

Outcomes included patient-reported measures of pain (numeric pain rating scale (NPRS); 0 to 10) and quality of life (Knee Injury and Osteoarthritis Outcome Score (KOOS) survey), manual assessment of knee muscle strength (0 to 5), physical capacity (lower limb functional index (LLFI; percentage), 30 second chair stand test (number of full repetitions), timed-up-and-go (TUG) test (seconds), 40m walk test (40MWT; seconds), balance (TUG test), knee joint range of motion (degrees) and limb circumference (cm). Outcomes were measured at baseline (one week prior to knee replacement surgery), one day prior to surgery, 4 days post-operatively (the expected day of discharge from hospital), and at one, two, four and six weeks after hospital discharge. All participants completed a study diary to record treatment compliance, pain scores and analgesic medication use.

During the project, Participant 1 had her surgery postponed and re-scheduled twice and she was withdrawn from the study protocol. Participant 1 was keen to continue a modified maintenance PBMT schedule over the subsequent 54 days until the re-scheduled surgery. During this period, the participant continued PBMT once to twice weekly as desired and she maintained a study diary. For completeness, her initial pre-operative results are aggregated with those of the other participants. Participant 1 was re-assessed the day prior to her re-scheduled surgery, and she continued with daily PBM application for 1 week after discharge from TKA surgery. All other participants completed the study per protocol including all assessments. The results are presented descriptively with results for Participant 1 shown separately in each graph.

The study was approved by the Mater Misericordiae Limited Human Research Ethics Committee (HREC/MML/52845 (V6)).

3. Results

3.1 Participants

In the 3-month period available for undertaking the study, four patients waitlisted for TKA surgery by the study Orthopaedic Surgeon complied with eligibility criteria and consented to participate in this feasibility study after responding to a recruitment package mail out. Table 1 shows the demographics and baseline characteristics of the participants [mean age 69.3 years; standard deviation (SD) 1.88].

Table 1 Demographics and baseline characteristics of the participants.

Participant	Age (years)	Gender	Affected leg
1	68	Female	Left
2	68	Female	Left
3	72	Female	Right
4	72	Female	Right
Mean	69.3	100% Female	50% Left 50% Right

3.2 Acceptability, Tolerability

Participant acceptability of the study methods was assessed by asking participants about their experiences of the research. On being surveyed, participants reported that: (1) they would 'definitely' like to have access to the light patch system if they needed joint replacement surgery in the future; (2) they would recommend the light patch system to a friend; (3) the system was comfortable to wear and reduced their pain; and (4) the testing protocol was 'about right' (with relevance to their condition and length of time to carry out physical assessments and questionnaires).

3.3 Adverse Effects

No adverse effects were reported by the participants during or after the intervention phases of the PBM device.

3.4 Numeric Pain Rating Scale (NPRS)

3.4.1 Participants 2, 3 and 4

Figure 2 (panels A to E) demonstrates the mean self-assessed NPRS during rest and functional activities from the start of the study at baseline (7 days prior to TKA) until 6 weeks after discharge from hospital. Patient-reported pain on activity commences in the moderate (4 to 6 out of 10) to severe (7/10 to 10/10) range at baseline for all activities, to low (1/10 to 3/10) by Day 4 post-operatively and nil pain by Week 6 after discharge.

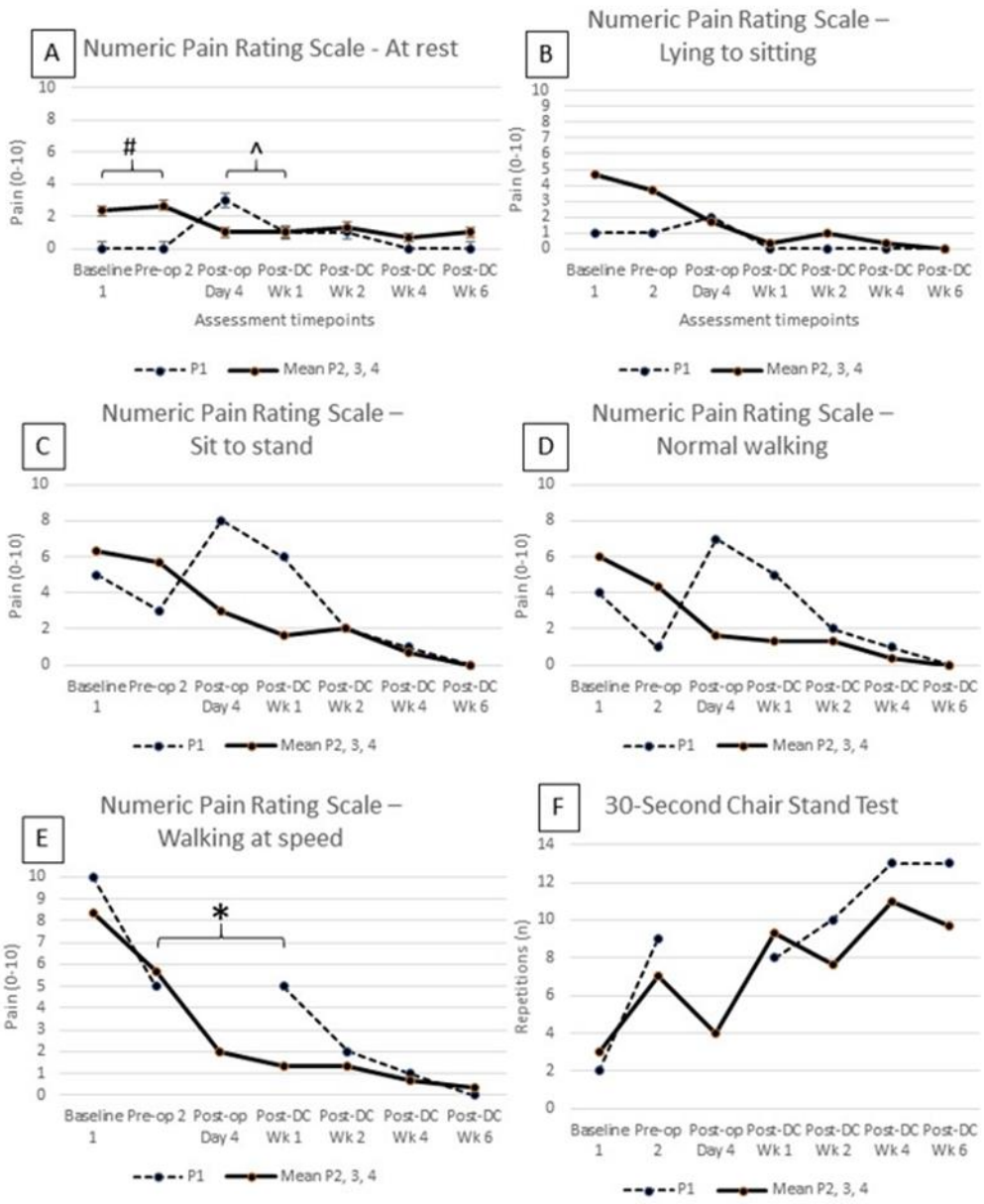

Figure 2 Numeric pain rating scores (NPRS) for different activities (panels A to E) and 30-second chair stand test (panel F) across all assessment time points.

3.4.2 Participant 1

Participant 1 whose pre-operative protocol was disrupted by 2 consecutive postponements of surgery, reported severe pain (7 to 10) on some functional tasks (Figure 2) post-operatively and was unable to complete the 40m walk test on Day 4 following surgery, due to the severity of pain thus there is no pain rating for fast walking for this participant on that day.

For all graphs, the period indicated by # = Daily PBM therapy for one week prior to surgery; and the period indicated by ^ = 2nd-daily PBM therapy for one week after discharge from hospital. *= gap between pre-operative assessment time and one week after hospital discharge representing the inability by Participant 1 to comply with 40m fast walk and 30-second chair stand tests on Day 4 post-op. [NPRS 0=no pain; NPRS 10=worst pain imaginable; Baseline1= one week prior to knee

replacement; Pre-op2= one day prior to knee replacement; Post-op Day 4= 4th day following surgery; Post-DC Wk1= one week after hospital discharge; Post-DC Wk2= two weeks after hospital discharge; Post-DC Wk4= four weeks after hospital discharge; Post-DC Wk6= six weeks after hospital discharge; P1= participant 1; P2, 3, 4= participants 2, 3 and 4].

3.5 30-Second Chair Stand Test

3.5.1 Participants 2, 3 and 4

The participants who completed the study per protocol recorded a progressive increase in the number of sit-stand-sit repetitions over the 30 seconds of the Chair Stands test (Figure 2, panel F) although the progress was irregular and did not follow the trend of the pain scores.

3.5.2 Participant 1

Participant 1 was unable to complete the 30-second Chair Stand test on Day 4 following surgery, due to the severity of pain including mild (1 to 3) pain at rest.

3.6 Muscle Strength Affected Knee

3.6.1 Participants 2, 3 and 4

Mean muscle strength (Figure 3, panel A) in the affected knee gradually progressed to 'normal' (Grade 5) by Week 4 post-discharge and was maintained when re-assessed at Week 6 follow-up.

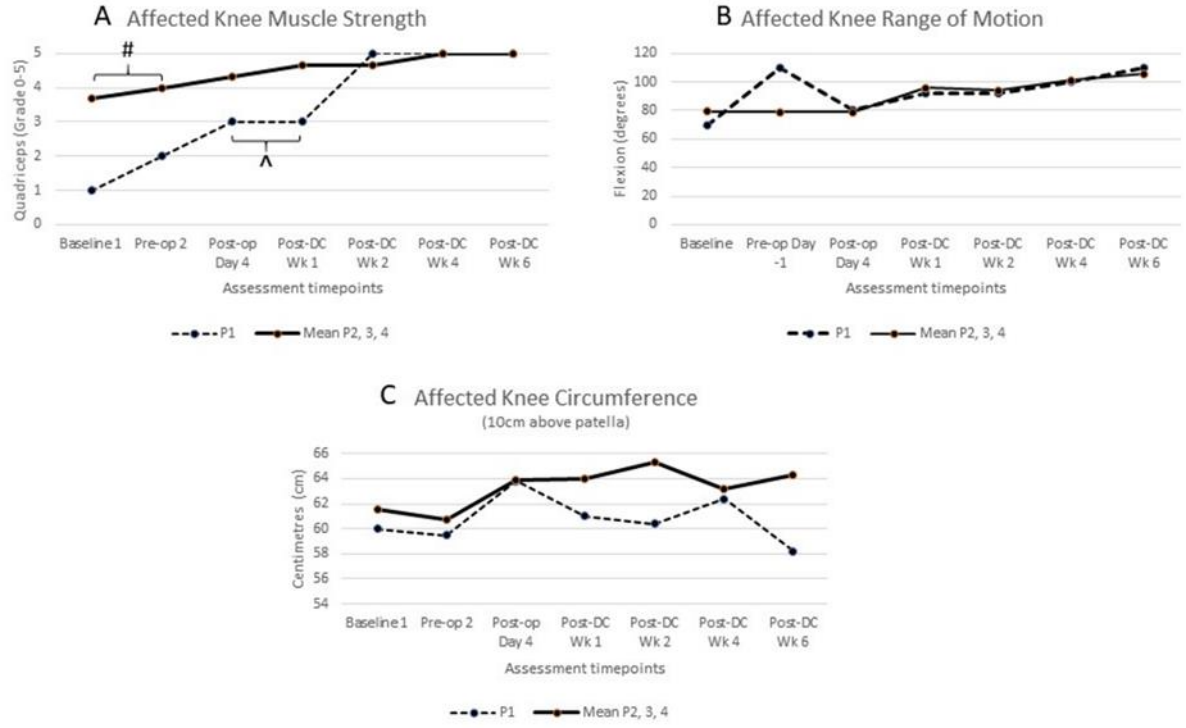

Figure 3 Knee extensor muscle strength (panel A), knee flexion range of motion (panel B) and knee circumference (panel C) of the affected operated limb across all assessment time points.

3.6.2. Participant 1

Muscle strength started at a low level (Grade 1) at baseline assessment and, despite the disruption to the treatment protocol and significant pain at Day 4 post-operation, Participant 1's muscle strength returned to Normal (Grade 5) by the second week after discharge.

For all graphs, the period indicated by #= represents daily PBM therapy for one week prior to surgery; and the period indicated by ^ = 2nd-daily PBM therapy for one week after discharge from hospital. [Baseline1= one week prior to knee replacement; Pre-op2= one day prior to knee replacement; Post-op Day 4= 4th day following surgery; Post-DC Wk1= one week after hospital discharge; Post-DC Wk2= two weeks after hospital discharge; Post-DC Wk4= four weeks after hospital discharge; Post-DC Wk6= six weeks after hospital discharge; P1= participant 1; P2, 3, 4= participants 2, 3 and 4].

3.7 Knee Flexion Range of Motion (Operated Leg)

3.7.1 Participants 2, 3 and 4

Mean knee flexion range of motion (Figure 3, panel B) in participants who progressed per protocol improved as expected for patients following TKA.

3.7.2 Participant 1

Participant 1 experienced an increase in knee flexion range of movement after the initial week of daily PBM. Post-operatively, her range of movement progressed to a similar and acceptable degree as the other participants by Week 6.

3.8 Knee Circumference (Operated Leg)

3.8.1 Participants 1, 2, 3 and 4

Knee circumference (measured at a point 10cm above the superior margin of the patella) (Figure 3, panel C) was variable at all time points; and a similar variability was demonstrated at the other measurement sites (not shown: 20cm above the patella, at the joint line and 5cm below the inferior pole of the patella).

3.9 Lower Limb Functional Index (LLFI)

3.9.1 Participants 2, 3 and 4

The mean measures of LLFI (Figure 4, panel A) demonstrated a progressive and steady improvement in the per protocol participants except for a small reduction at Week-2 after discharge.

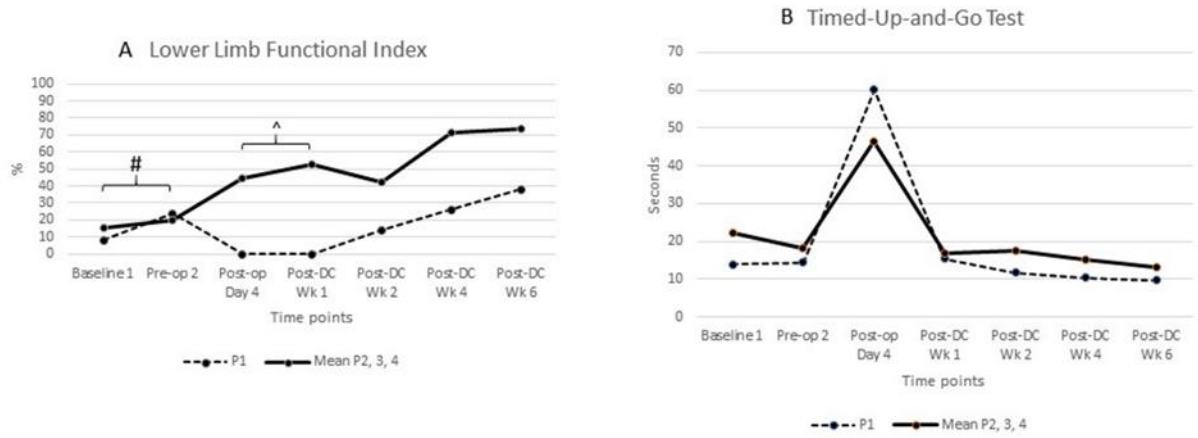

Figure 4 Lower limb functional index (panel A), and Timed-Up-and-Go test (panel B) across all assessment time points.

3.9.2 Participant 1

The LLFI in the participant whose intervention protocol was disrupted by postponed surgeries did not demonstrate the same self-assessed functional gain until later in her post-op recovery.

For all graphs, the period indicated by # = represents daily PBM therapy for one week prior to surgery; and the period indicated by ^ = 2nd-daily PBM therapy for one week after discharge from hospital. [Baseline1= one week prior to knee replacement; Pre-op2= one day prior to knee replacement; Post-op Day 4= 4th day following surgery; Post-DC Wk1= one week after hospital discharge; Post-DC Wk2= two weeks after hospital discharge; Post-DC Wk4= four weeks after hospital discharge; Post-DC Wk6= six weeks after hospital discharge; P1= participant 1; P2, 3, 4= participants 2, 3 and 4].

3.10 Timed-Up-and-Go (TUG) Test

3.10.1 Participants 1, 2, 3 and 4

Despite the expected effect of surgery on time taken to complete the TUG test at Day 4 post-surgery in all participants (Figure 4, panel B), by Week 6 follow-up, the time taken to complete the test had improved with an average overall improvement of nearly 10 seconds. At baseline, the mean time for completing the TUG test in participants 2, 3 and 4 (who completed all study requirements per protocol) was 22.27 s (range 16.93-27.95 s). At 6 weeks, the mean time for completing the test for the same participants was 13.3 s (range 10.23-18.25 s). The results for Participant 1 were reflected in the mean results for the other participants.

3.11 Opioid Requirements

On Day 1 after surgery, our participants required an average daily opioid equivalent dose of 33.75mg compared to a historical matched control group of 38.93mg. On Days Two to Four, the historically matched controls required an average daily opioid equivalent dose of 45.42 mg compared to the PBM group of 70mg. We found from the study diaries that after discharge from hospital, our participants primarily managed their pain using simple analgesia (such as

paracetamol) rather than potentially addictive opioids. No data for post-discharge analgesic requirements was available for the matched control group.

4. Discussion

The primary aims of this n=4 feasibility study were to determine whether PBM as applied using the novel light patch system self-administered in the patient's home before and after TKA surgery would be acceptable and tolerable to patients; and determine if the intervention could influence pre- and post-operative pain, functional recovery, and opioid analgesic requirements. Each of the aims was at least partially achieved. Participants found the PBM device used in the study was comfortable to wear, reduced their pain, and none experienced any adverse effects. We were unable to make comparisons of opioid consumption between participants in this study and a historically matched control group. The authors recognize that the results of such a small study cannot be generalized to the broader population. Although only a small sample, the magnitude of perceived benefit and improvement in pain and physical measures was sufficient to confirm the need for an adequately powered, randomized and placebo-controlled clinical trial.

The mean pre-operative pain scores for our participants were similar to those reported by Phillips et al [14] in a study of 96 patients undergoing TKA for KOA. All of our participants reported no (zero) pain in all functional tests assessed in the study at the 6-week post-discharge follow-up assessment. There were no reports of neuropathic pain at 6-week follow-up when it can be most prevalent [14]. It is reasonable to expect that Day 4 post-operative reports of pain would be greater than pre-operative reports, yet this was only evident in Participant 1 whose protocol was interrupted by cancellations of her surgery. Her inability to comply with some of the functional testing is explained by her reports of pain and poorer muscle strength.

As none of our participants reported any pain at the formal 6-week follow-up assessment nor at 3- and 6-month clinical follow-up, we feel confident that our feasibility study supports the potential for further research. Our preliminary data are impressive considering other research of the natural history of pain after TKA. For example, Phillips et al [14] reported mean pain scores of 3.2/10 at 6 weeks; two-thirds of patients continued to report pain at 9 months follow-up; and only 45% had no pain at 46 months follow-up. In the largest study of its type, a prospective study of recovery after knee replacement surgery [15], the authors followed 494 patients for one year and collected outcome indicators of pain and function pre-operatively and at 2 weeks, and 1, 3, 6 and 12 months. The mean pain scores reported by Davis et al [15], on the KOOS survey were 5.2 out of 10 (SD 1.2) at 2 weeks after knee replacement surgery, 3.6 out of 10 (SD 1.7) at 1 month, and 2.4 out of 10 (SD 1.7) at 3 months. Participants continued to report mean pain scores of 1.7 out of 10 (SD 1.6) at 12 months. The same authors reported that participation restrictions increased during the first 4 weeks after TKA before improvement began and the restrictions may have been accounted for by fatigue, anxiety, depression, and post-operative pain scores. We did not encounter such factors in our small group of participants. Although the data collection points used by Davis and colleagues were different to those used in our feasibility study, the findings suggest that the outcomes of our feasibility study, if replicated in a large, randomized placebo-controlled clinical trial, have the potential to impact this field of surgery.

As no PBMT was applied for any participants during the immediate post-operative hospital admission period, the results are more likely to reflect the post-op analgesic regimen in place at

the time of the study. It would be interesting to see in future research, if PBMT pre-operatively and in the immediate post-op period influences analgesic requirements whilst patients are in hospital; and if length of hospital stay changes as a result. If post-operative pain can be adequately controlled in the immediate post-operative period, and patients could continue applying non-pharmacological PBMT on return home after surgery (without risk of adverse effects of pharmacological analgesics), length of stay and hospital costs might be reduced. We aim to measure direct and indirect costs in a follow-up study.

The reduction in pain scores for all functional activities (changing position from lying down to sitting, from sitting to standing, when walking normally and when walking at a fast pace) in all participants in the week between baseline (initial) assessment and the day before surgery is notable. Participants used the device daily for 30 minutes during that period. This outcome raises the prospect that PBM could be investigated in future research for its effects in severe grade KOA with the potential to delay or prevent the need for costly joint replacement surgery. As pain reports and physical measures improved in the pre-operative week, we can propose that the pre-conditioning regimen was effective in influencing pain and muscle activity that may have optimized some of the post-operative outcomes. This proposition can be tested further in future research. If the same results are identified in an adequately powered randomized placebo-controlled clinical trial of PBMT, the outcomes would support other literature of the use of PBMT in KOA of lesser severity [1]. In the TKA setting, the minimal clinically important difference for pain scores is between 1.5 and 3 points depending on the study [16] and this was achieved in all our participants on all functional tests.

The difference in opioid ingestion (morphine equivalency) on post-operative Days 2 to 4 between the historically matched controls and the participants in the feasibility study can be explained by Participant 2 who required markedly more pharmacological analgesia than the other participants during their hospital stay. Participant 2 accounted for almost all (98.8%) of the opioid analgesic requirements across all participants on Days 1, 2 and 3 after surgery but by Day 8 following surgery, she no longer required any opioid analgesia.

Moderate to severe postoperative pain, particularly after orthopaedic procedures, remains one of the highest causes of significant physical dysfunction and impaired rehabilitation and recovery in patients undergoing a surgical procedure, causing additional long-term effects after discharge that can significantly reduce a patient's quality of life. Despite several studies indicating the benefits of PBM as a therapeutic adjuvant in pain management, there is a continued reliance on post-operative pharmacological agents, including opioids, gabapentinoids, local and regional anaesthetics, and non-steroidal anti-inflammatory drugs. Such agents often suffer from short duration of analgesic effect, detrimental side effects and the possibility of addiction, misuse and abuse with prolonged use. These factors can result in significant morbidity and mortality separate from the risk factors associated with surgery itself. A future study will more closely examine participant opioid requirements over a 12-month follow-up period to see if PBMT is a viable alternative to opioids after knee replacement surgery.

Although there was some variability in improvement in the 30-second chair stand test (number of repetitions) over the duration of the study, the mean number of repetitions achieved by the participants by Week-6 follow-up was approaching age- and sex-referenced norms. The chair stand test is a measure of leg strength in older adults. In a study of community-dwellers, Rikli and Jones [17] reported age-referenced chair stand test norms for women of 65 to 69 years old as 13.5

repetitions, and women of 70 to 74 years as 12.9 repetitions. Our study results are reflected in the measures of muscle strength which had returned to normal (Grade 5, defined as maintaining an end point range (break testing) against maximum resistance) at 1 month after surgery in all participants. The chair stand test results are likely to have improved in parallel with the noted reductions in the measures of pain when transferring from sitting to standing (Panel C, Figure 2).

Knee circumference was measured at four sites (at the joint line and above and below the knee) as a de facto measure of limb swelling. Figure 3 (Panel C) demonstrates variability in these measures at the joint line, indicating that knee circumference measures using a tape measure cannot be used as a reliable indicator of inflammatory swelling in future studies. Other methods such as bioimpedance (that can be used in the home setting) would need to be considered in future research.

In our study, all participants were able to attain at least 80 degrees knee flexion range of motion on discharge from hospital. The benchmark of knee flexion range of motion for hospital discharge in Australia has generally been ≥80 degrees but with increasing patient numbers having knee replacement surgery, and hospital bed availability pressures, Naylor et al [18] found that only 2% of 176 patients in benchmarked hospitals were able to attain ≥80 degrees knee flexion even where length of hospital stay was greater than 4 days. Our results suggest that this measure is worth assessing in future studies as a possible benefit of treatment with PBM.

The TUG test results also demonstrated favorable outcomes. Although still considered worse than average in our feasibility study, times for completion of the test trended steadily toward the age-referenced norm for this test (8.1 s for 60–69-year-old adults, and 9.2s for 70–79-year-old men and women [19]). The marked reduction in time taken to perform the TUG test between post-op Day 4 (when times were at their worst during the immediate post-operative phase) and 7 days later (at one week after hospital discharge) reflects positively on the PBM intervention. In circumstances where knee pain was reportedly zero out of ten at 6 weeks, it is expected that there would be further improvement in the TUG test over time as patient confidence improves. Moreover, the effect of PBM on pain and TUG testing during the immediate post-operative period whilst in hospital would be worthwhile understanding. These factors will be assessed over a longer follow-up period in a future study, after commencing the intervention on Day 1 post-operatively.

The LLFI is considered viable for evaluation of lower-limb status and impairment in clinical and research settings due to its improved responsiveness and overall performance compared with other measures [20]. Our results demonstrated progressive improvement in patient-reported function over time. In future research, we aim to compare function between active and placebo treatment groups over a 12-month time frame to better understand the effect of the PBM intervention.

There is great diversity in PBM protocols and results of studies that have used the therapy for common musculoskeletal conditions. It is instructive to understand why PBM might be useful in the peri-operative setting in which this feasibility study was based. Photons, once applied to tissues, deliver light energy that is absorbed by chromophores, which in turn initiate a cascade of molecular reactions leading to cell proliferation and have been shown to modulate the inflammatory process and reduce pain (e. g., Hamblin [21]). The analgesic properties of PBM therapy have been investigated and supported over many decades [22] with several studies reporting significant analgesia in a variety of acute and chronic orthopaedic and musculoskeletal conditions. In translational research by Zupin et al [23], the authors showed that 800 nm PBM

acted on mitochondrial dysregulation, increasing levels of reactive oxygen species and mitochondrial membrane potential; and 900nm PBM acted on nociceptive signal transmission. Chow et al [24] demonstrated the analgesic effect of photonic energy in dorsal root ganglia. The results on pain reports in our feasibility study are not unexpected considerate of the evidence in the basic science literature, yet such factors have not been fully verified in clinical studies.

PBM has been investigated for its effects on soft tissue and bone tissue healing mainly in animal and dental settings. In a meta-analysis of bone healing in animals, the authors [25] identified enhanced bone strength in fracture healing models suggesting that human trials were warranted. In a systematic review of animal and human studies of osseointegration and bone graft regeneration, Zein et al [26] identified consistent reports of increased cellular metabolism and increased protein synthesis using PBM. In another systematic review of bone healing after tooth extraction, no side effects of PBM were reported; and there were higher concentrations of osteogenic markers (Ocn and Runx2) consistently reported as well as higher percentages of bone trabeculae and bone density in tissues submitted to PBM [27]. Many anti-inflammatory and angiogenic genes have been found to express in response to PBM in bone research (e. g., up-regulation of MMD, PTGIR, PTGS2, IL1, IL6, IL8, IL18, FGF14, FGF2, ANGPT2, ANGPT4, PDGFD) and higher expression of COX-2 and VEGF [28]. Bone repair has been found to accelerate [29] and bone implant integration has been demonstrated in a primate model [30]. In an animal model of induced OA, the authors [31] found that 660nm and 808nm PBM resulted in proliferation of blood vessels and epitheloid cells in cartilage; and there was greater production of fibrotic tissue in the control animals. Causes of continuing pain after joint replacement surgery are largely unknown but may be due to prosthetic loosening and instability, thus the potential for PBM in preventing or limiting such factors is intriguing. Although this feasibility study was not designed to investigate such effects, we will evaluate the effects of PBM in human bone, cartilage, and synovial tissue in a future study to determine whether soft and hard tissue healing may contribute to outcomes such as reduced pain and optimal prosthetic stability. Due to the growing evidence that the effect of PBM may be wavelength dependent we determined at the outset of this study that a device that combined both visible and infrared wavelengths of light energy, should deliver the anti-inflammatory and analgesic effects of PBM in a clinical surgical model.

The main strength of this study was its pragmatic design that reduced the burden on hospital staff in its implementation. The study has permitted the researchers to understand which aspects can be progressed with in a future clinical trial, and which aspects should be modified. The lack of gender diversity and the small number of participants in this study were the main limitations but as the study was designed to test the feasibility of the protocol, methods, and acceptability of the intervention by the target participant group, we have only been able to describe and interpret the results in that context. It was not possible to adequately measure post-hospital discharge opioid analgesic requirements in historically matched controls due to lack of information for the control group. The veracity and reliability in use by the participants of the study diary could not be verified and future studies will need to take account of this aspect. The KOOS data was unreliably reported with many missing data points across most domains at all measurement points for all participants, therefore quality of life was not able to be assessed accurately in our study. Future studies of this type in older adults, may be better served by using the short form KOOS-PS [32] or another quality-of-life measurement instrument.

5. Conclusions

The study of a novel PBM light patch system that could be self-administered in the patient's home before and after TKA surgery was found to be feasible, and the device acceptable to participants. Pre- and post-operative pain and post-operative functional recovery was positively influenced by the intervention. It was not possible to determine the effect of the intervention on opioid requirements post-operatively. No adverse effects were observed or reported. The researchers will use the outcomes of this feasibility study when designing and proceeding to a larger, adequately powered study.

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Author Contributions

PGV and E-LL are responsible for the implementation of the study protocol and data collection. LL was primarily responsible for data analysis. PGV and E-LL were responsible for the drafting of the manuscript. Both authors contributed to and approved the final manuscript.

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Competing Interests

The authors declare no conflict of interest.

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