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The IlluminOss® System: a solution in elderly patients with upper limbs bone metastases

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Abstract. – OBJECTIVE: The IlluminOss® System (IS) based on photodynamic bone stabilization (PBS) is a recent option in between the minimally invasive surgical techniques available to treat bone metastases when medical or radiation therapy is neither effective nor indicated, and major surgery is not possible. In this study, the results obtained using IS in the treatment of impending fractures or bone metastases of the upper limb have been analyzed in terms of improvement in pain, quality of life and recovery of function.

PATIENTS AND METHODS: Between January 2017 and October 2019, 8 patients over 65 years old with impending fractures or pathological fractures or myeloma of the upper limb have been treated in our institute with IS. All patients were assessed about pain, general health and function of the affected limb before surgery and 1, 3, 6 (consistent with survival) months after the procedure.

RESULTS: Mean VAS score improved from 8.88 before surgery to 1.00 six months after surgery, mean Karnofsky index improved at 1 and 3 months post-operative follow-up, and Musculoskeletal Tumor Society Score (MSTS) raised from 44.6 before surgery to 74.7 six months after surgery. Moreover, good reduction and stable fixation of the osteolytic lesion were achieved in all patients, and no complications were found.

CONCLUSIONS: Numerous studies have been reported in the literature on the use of this system in osteoporotic elderly fractures, whereas only few articles are currently available regarding its use in the treatment of bone metastases or pathological fractures. From our study PBS seems to be an effective solution in the management of bone metastases or myeloma in both pathological fractures and impending upper limb fractures in patients with low life expectancy.

Key Words:
Bone metastasis, Palliative treatment, IlluminOss® System, Pathologic fracture, Poor prognosis, Photodynamic Bone Stabilization, Impending fracture.

Introduction

The treatment of bone metastases is still a great challenge today[1,2]. The need to stabilize bone metastases remains controversial in patients with short life expectancy due to advanced cancer[3]. Whenever medical or radiation therapy is neither effective nor indicated, and major surgery is not possible, palliative and minimally invasive surgeries can be proposed to the patient[1,4]. Minimally invasive surgical techniques as cementoplasty[5,6], ethanol injection, cryoablation, electrochemotherapy, high intensity radiofrequency ablation, and photodynamic bone stabilization are finding more and more indications over the years due to the numerous advantages: small surgical access, reduced hospital stay, low morbidity, good results and reduced costs[7-10].

The Photodynamic Bone Stabilization (PBS) is a recent option for intramedullary stabilization of bone fractures and forms a customized implant using a light-cured polymer contained within an inflatable balloon catheter[11] which poses additional problems for surgical repair due to increased intramedullary volume. Treatment with internal fixation using intramedullary nails or plating is associated with poor clinical outcomes in this patient population. Subsequent fractures and complications such as screw pull-out necessitate additional interventions, prolonging recovery and increasing health care costs.

Due to its characteristics, PBS represents an option of indisputable value for the treatment of fractures in pathological bone (such as lytic metastatic ones or other bone lytic lesion) in which biology is severely impaired and life expectancy is relatively short.

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The IlluminOss® System (IS – IlluminOss® Medical, Inc., East Providence, RI, USA) received European regulatory approval (CE mark) in 2009 and is indicated for use in the reduction and alignment of fractures with no or low load bearing[12].

In this study, we reported and analyzed the results obtained, using the IS in the treatment of impending fracture or bone metastases and lytic lesion in patients affected by myeloma in the upper limb, in terms of improvement of pain and quality of life, restoration of function of the treated segment and resumption of activities of daily living.

Patients and Methods

A retrospective observational study according to the STROBE guidelines[13] (STROBE Checklist in **Supplementary Table I**) was conducted.

All patients treated with IS, between January 2017 and October 2019, in our department have been retrospectively reviewed.

Inclusion criteria were: patients older than 65 years and with bone metastases (with pathological or impending fracture) of the upper limb. Exclusion criteria were: patients younger than 65 years of age and treated with IS for diagnosis other than bone metastases. The choice of IS as treatment depended on surgeons' preference and on patient status as they were all plurimetastatic and with impending or minimally displaced fracture not responding to local radiotherapy (RT).

The results were retrospectively reviewed using hospital and patient operations charts. Medical records were reviewed to gather information including patient and primary tumor characteristics, surgery details and surgical outcomes. The outpatient records were reviewed for post-operative follow-up.

Standard radiographs or CT examination, when already performed for other clinical reasons (for example, disease staging), were used for the preoperative and postoperative evaluation of bone lesions.

The primary outcomes of the study were the assessment of improvement in pain, quality of life and function of the operated limb. The incidence of adverse effects or complications, surgical revision rate, hospital stay, and survival were also evaluated.

All patients were assessed about pain, general health and function of the affected limb before surgery and 1, 3, 6 (consistent with survival) months after the procedure.

The severity of regional pain was measured by a Visual Analog Scale (VAS)[14] ranging from 0 (no pain) to 10 (worst pain). The overall performance status was assessed through the Karnofsky score[15]. The functional outcomes for the upper limbs were objectively assessed through the Musculoskeletal Tumor Society for upper extremities score (MSTS-ue)[16].

Surgical Technique

The device consisted of an intramedullary balloon catheter, a fiber optic light tube, a photodynamic liquid monomer and the related control technology. After reduction of the fracture, the balloon was inserted into the intramedullary space through a small percutaneous incision.

For the humerus, the incision was like the one used for anterograde intramedullary nailing; regarding the radius, the incision was made dorsally at the distal epiphysis. The balloon was available in sizes ranging from 40 to 280 mm in length and 4 to 22 mm in diameter, with volume ranging from 5 to 51 mL. Once properly positioned, the balloon was infused with a biocompatible photodynamic liquid monomer and, after ensuring proper alignment, the fiber optic light tube was inserted through the inner lumen of the balloon. The light tube was controlled by the surgeon *via* an external console and a timer button that quickly cured the liquid, forming a strong and hardened bone stabilizer bar. The monomer took between 200 and 800 seconds to cure, depending on the volume. The balloon was positioned across the fracture and once cured, provided both longitudinal and rotational stability due to its ability to fully contact the cortical wall.

Despite this structural stability, the cured monomer provided an excellent substrate into which screws could be inserted for additional stability.

Postoperatively, patients with humerus fracture wore a pocket brace while those with radius fracture wore a plaster splint for 3 weeks. All patients started active and passive mobilization of the upper limb joints, with a specialized physiotherapist, from the first post-operative day.

Statistical Analysis

Given the small number of patients included in the study, the statistical analysis was limited to a descriptive statistic. Statistical analysis was performed using SPSS 18.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

The demographic characteristics of the patients included in the study are reported in Table I. Eight patients (4 men and 4 women; mean age, 72 years; range, 66-79 years) underwent the PBS index procedure (Figure 1).

All patients, with a known history of cancer, came to our attention for pain and severe functional limitation to the upper limb. Four patients had a medical history of multiple myeloma (MM), three of clear cell renal tumor and one of papillary bladder carcinoma. After physical examination of the affected limb and evaluation of standard radiographs or CT scans, 8 osteolytic lesions localized in the bones of the upper limb were detected. Left side was affected in 5 cases, right side affected in 3 cases.

The proximal humerus was involved in six cases and the proximal radius in two cases. Two patients had an impending fracture of the proximal humerus, while the other 6 already had a pathological fracture in progress (4 of the humerus and two of the radius). All patients had multiple bone and/or visceral metastases and were evaluated by a multidisciplinary team. All patients had already performed RT both for the bone localization under examination and for other disseminated sites, and for other parenchymatous organs. The 4 patients with MM had undergone chemotherapy (CT) and bone marrow transplantation.

Surgical Information

Six patients were operated in the semi-sitting position (beach chair) and the two with a fracture of the proximal radius in supine decubitus. General anesthesia was performed in 4 patients, whereas 4 patients with humerus fracture were operated under interscalene block.

After closed reduction of the fractures under fluoroscopic control and after taking bone material for biopsy, PBS was performed with a percutaneous procedure, according to the technique described above. No screws or additional hardware were used for internal fixation in any patient.

The mean operative time from skin incision to closure was 65.25 min (range, 53-78 min). There was no need for post-operative red blood cell transfusions, patients went from a mean pre-operative Hb of 10.4 g/dL (range 8.6-12.8 g/dL) to a mean Hb in the first postoperative day of 10.3 g/dL (range 8.7-12.4 g/dL). Furthermore, no patient required post-operative intensive care. In the post-operative phase, patients were encouraged to actively and passively mobilize the joints of the upper limb immediately, with pain tolerance.

Primary Outcomes

The mean preoperative pain for the 8 patients was 8.88 on the VAS scale (range 7.0-10.0) (Table 1). Marked pain palliation was observed 1 month after surgery with a mean of 4.63 (range 3.0-6.0). The pain level further improved at 3 and 6 months after surgery (mean 2.0 and 1.0, respectively). At 6 months, two patients reported complete disappearance of pain in the treated surgical site (Figure 2).

The general performance status, measured with the Karnofsky index, also showed an improvement from preoperative to 1 and 3 months postoperative, passing respectively from 33.8 (range 10.0-50.0) of the preoperative, to 46.3 (range 20.0-70.0) at one month and to 63.8 (range 50.0-70.0) at 3 months. Worsening of the general condition was observed 6 months after the surgery, with an average score of 53.8 (range 0.0-80.0), but this parameter is strongly influenced by the death of 2 patients at 4 and 5 months (Figure 3).

As for the MSTS-upper extremities functional score, it improved slightly one month after surgery, from 44.6 (range 35.0-51.0) in the preoperative period to 55.5 (range 44.0-64.0). While a more relevant functional improvement occurred 3 months after surgery (mean 71.5; range 63.0-84.0). At 6 months, the MSTS functional score in the 6 patients still alive showed another small improvement (mean 74.7; range 65.0-83.0) (Figure 4).

Other Outcomes

Good reduction and stable fixation of the osteolytic lesion was achieved in all patients, with bone healing within 3 months. No surgical wound problems and extravasation of the polymer from the bone was found. No implant failure and further osteolysis of the treated bone were observed in the remaining survival period. None of our patients required any further surgery. The mean hospital stay was 2.5 days (range 2.0-5.0 days). The mean survival in our patients was 17.1 months (range 4.0-35.0 months). Two patients died within 6 months, one from cerebral hemorrhage and one from pulmonary complications, while 4 patients had a survival of more than 2 years. The one-year survival rate was 50% (4 of 8 patients).

Table I. Patient demographic characteristics.

Case	Sex	Age	Bone location	Primary cancer	Clinical presentation (impending/ pathological fracture)	Surgery duration (minutes)	VAS (pre/1/3/6 months)	Karnofsky (pre/1/3/6 months)	MSTS-ue (pre/1/3/6 months)	Hospital stay (days)	Survival (months)
1	M	77	Left proximal radius	Papillary bladder	Pathological	71	10/6/2/-	10/30/50/0	35/44/66/-	2	4
2	F	68	Left proximal humerus	MM	Impeding	60	8/3/1/0	50/70/80/80	51/55/63/83	4	33
3	F	79	Right proximal humerus	MM	Impeding	68	7/4/1/1	50/50/70/70	45/60/72/80	2	35
4	M	77	Left proximal humerus	Clear cell renal	Pathological	61	9/5/3/-	20/20/50/0	42/64/76/-	3	5
5	M	69	Right proximal humerus	Clear cell renal	Pathological	78	10/6/3/2	30/50/60/70	45/53/68/65	2	8
6	F	67	Left proximal humerus	MM	Pathological	53	9/4/2/1	40/60/70/70	50/57/84/71	2	18
7	M	73	Right proximal humerus	Clear cell renal	Pathological	66	9/5/3/2	50/60/70/70	44/55/71/75	3	10
8	F	66	Left proximal radius	MM	Pathological	65	9/4/1/0	20/30/60/70	45/56/72/74	2	24
Mean		72				62.2	8.9/4.6/2/1	33.8/46.3/63.8/53.8	44.6/55.5/71.5/74.7	2.5	17.1

M: Male; F: Female; MM: Multiple Myeloma; VAS: Visual Analog Scale; MSTS-ue: Musculoskeletal Tumor Society for upper extremities score.

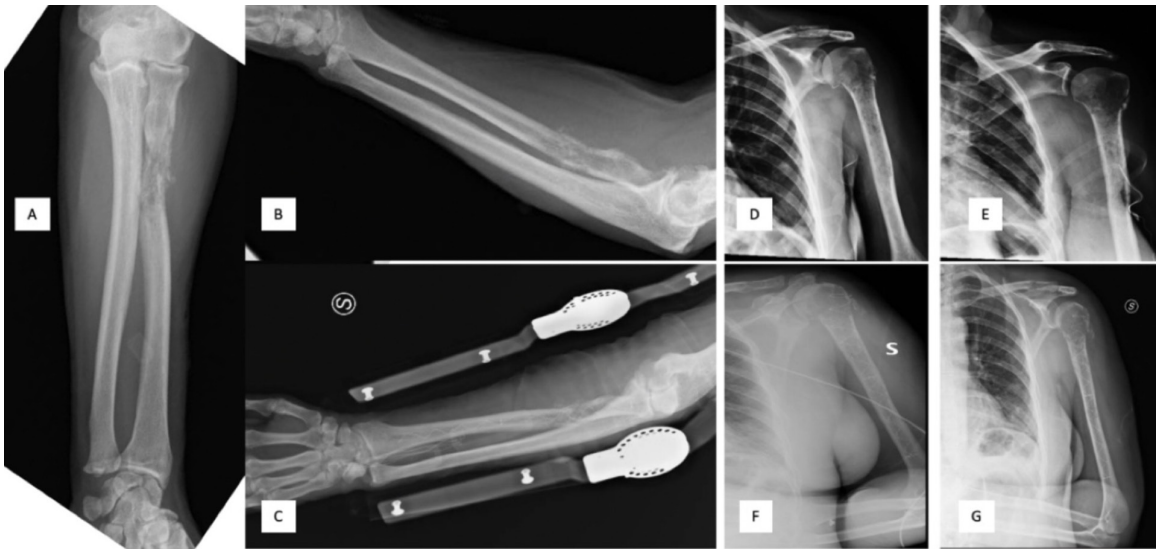

Figure 1. Pre **(A-B)** and post-surgery **(C)** x-ray of a patient with pathological fracture of the left radius (case 1 of this series). Pre **(D-E)** and post-surgery **(F-G)** x-ray of a patient with pathological fracture of the left proximal humerus (case 6 of this series).

There was much difference between the 4 myeloma patients, with a longer median survival (mean 27.5 months; range 18.0-35.0 months) compared to the 4 patients with genitourinary tract tumors who had a mean survival of 6.8 months; range 4.0-10.0 months).

Discussion

The genesis of the PBS involves technology derivatives from a series of independent surgical technologies: catheters and balloons from interventional cardiology and interventional radiolo-

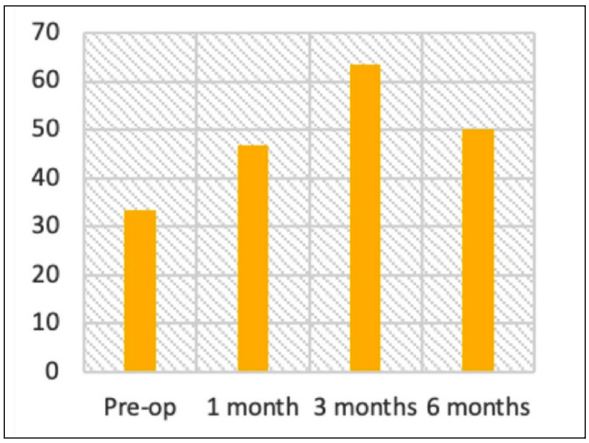

Figure 3. Trend of the mean Karnofsky score value.

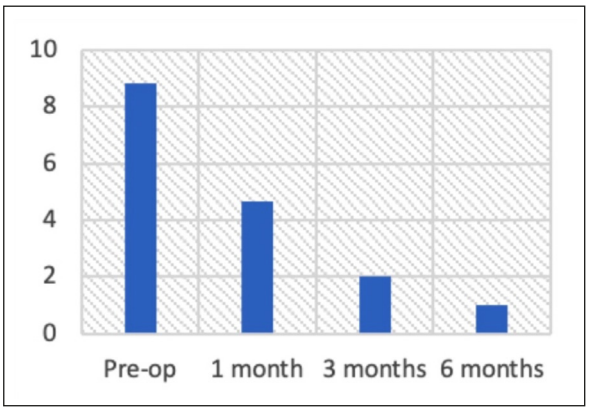

Figure 2. Trend of the mean VAS (Visual Analog Scale) value.

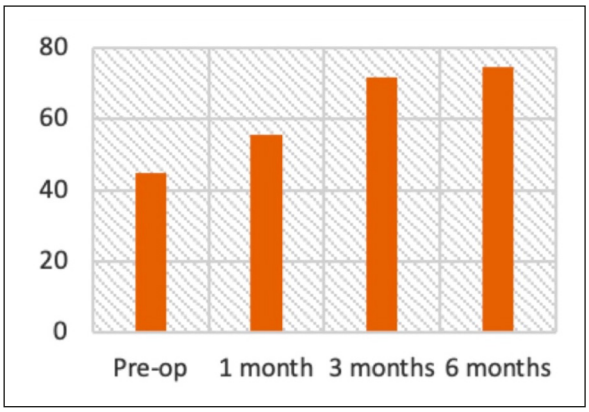

Figure 4. Trend of the average MSTS-ue (Musculoskeletal Tumor Society for upper extremities score).

gy, fiber optics from endoscopy, and monomers and polymers from dental cements[17]. This strategy combines the stability of intramedullary nailing with the versatility of balloon kyphosis techniques used in vertebral fracture repair. However, unlike vertebroplasty, the IS maintains the monomer within the confines of the balloon, eliminating the risk of extravasation[18]. Summarizing, the IS offers significant benefits to the orthopedic surgeons for the following reasons:

– it is minimally invasive;
– the monomer is infused and completely contained in the balloon;
– the balloon conforms to the medullary canal providing a custom-made intramedullary device;
– IS cures on demand only when visible light is applied, unlike rapidly hardening bone cement and it allows the surgeon the freedom and time to attain proper reduction of the fracture before hardening the polymer[19,20];
– it provides rapid stability and resistance to fracture and compromised bone;
– it is radiolucent for better visibility of the cortex;
– the radiopaque spiral markings provide a 3D profile of the implant;
– it can be used in conjunction with other devices for fracture fixation (hybrid osteosynthesis)[12] forming a patient customized intramedullary implant. A registry was established in Germany and The Netherlands to prospectively collect technical and clinical outcomes in patients treated with IS for fractures of the phalange, metacarpal, radius, ulna, distal radius, fibula, clavicle and/or olecranon. Humeral, femoral, tibial and pelvic fractures were included under compassionate use. Procedural success included successful placement of the device at the target fracture site and achievement of fracture stabilization. Clinical and radiographic assessments were made postoperatively through 12 months. One hundred thirty two patients (149 fractures.

Thus, IS represents a unique value for the treatment of fractures in compromised bone (osteoporotic fractures, pathological fractures and/or impending fractures) as it provides internal strength and stability to the weakened bone[21].

In the U.S.A., the IS is indicated for use in the treatment of traumatic, fragility, pathological, and impending pathological fractures of the humerus, radius, and ulna. Internationally, the IS is CE approved for use in the treatment of low-load bone fractures, as well as in the humerus for the treatment of impending fractures or pathological fractures.

A registry was established in Germany and The Netherlands to prospectively collect technical and clinical outcomes in patients treated with IS for fractures of the phalange, metacarpal, radius, ulna, distal radius, fibula, clavicle and/or olecranon[12]. 132 patients with 149 fractures have been enrolled in the registry and treated with the photodynamic bone stabilization system. Most patients (>80%) were older females who suffered a traumatic appendicular fracture.

Numerous studies[11,18,11-26] have been reported in the literature on the use of this system in osteoporotic elderly fractures (mainly upper limb including proximal humerus[11,18], distal radius[22,23], metacarpal fractures[24], pubic branches[25,26]).

The use in a case of osteogenesis imperfecta with injection into the femur and acetabulum is also reported[27].

The literature on its use in the treatment of bone metastases or pathological fractures is more limited, especially in a group of elderly cancer patients (age > 65 years) with such peculiar characteristics[28]. Fisher et al[29] reported several cases of vertebral metastases, describing PBS as an adjuvant for tumor ablation in minimally invasive procedures, such as vertebroplasty and balloon kyphoplasty.

Regarding long bone metastases, Albertini et al[1] presented a case report of a patient with a history of renal cell cancer presenting pathologic fractures of both humeri and proximal right radius. In this patient, PBS was associated with electrochemotherapy, reporting favorable results in terms of functional scores and pain well controlled with opioids.

Hoellwarth et al[30], in 2020, analyzed 105 pathological fractures of the humerus. Of these, only 19 were treated with PBS, while 65 with intramedullary nailing (IMN) and 21 with cemented plate fixation (CPF); at 2 years follow-up, no statistically significant differences were found in terms of reoperation rate between the 3 groups, but IMN surgery resulted in the lowest rate of broken implants (zero), statistically significant *vs.* PBS at all time periods and *vs.* CPF at final follow-up.

In another retrospective case series, Zoccali et al[31], reported similar results to ours in a case series of 12 patients. Also in this series, these were pathological or impending fractures of the upper limb (all in the humerus) but with a lower mean

age. The authors reported no intra- or post-operative complications and reported a significant improvement in pain (from 7 pre-operatively to 2.6 one month after surgery).

Limitations and Strengths

Our study had some limitations. First, it was a retrospective study. The number of patients was very small, and this did not allow a broad statistical analysis. Furthermore, there is a possibility that complications did not occur due to the small number of patients in the study population. Finally, there were no control groups, thus not providing a direct comparison with other types of treatment in the same patient typology.

The strengths of the study were the homogeneity of the type of fractures treated and the long follow-up. In addition, to the best of our knowledge, our study is one of the few in literature that analyzes this type of treatment in a group of patients with only bone metastases and pathological fractures.

Conclusions

In the surgical treatment of pathological fractures, the choice of an implant that allows immediate functional use of the limb and will last for the patient's lifetime is important. PBS requires little surgical access with minimal soft tissue injury, reducing surgical time and hospital stay. Despite the small number of cases in our study, and its retrospective design, PBS seems to produce good and effective results in the management of bone metastases or myeloma associated with both pathological fractures and impending fracture of the upper limb in multimetastatic patients with a low life expectancy by reducing pain, improving the quality of life and the general state of the patient.

Conflict of Interest

Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Not applicable.

Informed Consent

All procedures were performed following written informed patient consent and in accordance with the ethical standards of the institutional and national research committee and the 1964 Declaration of Helsinki. Patients were not required to provide informed consent to process data for the study because the analysis used anonymous clinical data.

Ethics Approval

The study design was approved by the Orthopedic Department council and our school board. As this was an approval from the Review Board of Orthopedic and Traumatology Institute there was no code. The approval date was the session of 24 May 2022.

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