First Human Use of SakuraBead, a resorbable embolic agent, in the treatment of pain secondary to Knee osteoarthritis

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Purpose

- Knee osteoarthritis (KOA) is a common progressive multifactorial joint disease and is characterised by chronic pain and functional disability which accounts for almost four-fifths of the burden of OA worldwide [1].

- Genicular Artery Embolization (GAE) has emerged as an effective treatment of KOA which resulted in a decreased need for pain medication for KOA, with a 27%, 65%, and 73% decline in the number of patients who used opioids, nonsteroidal anti-inflammatory drugs, and intra-articular hyaluronic acid injection, respectively [2].

- Clinical data has shown promise in reducing patient's pain and improving function using permanent embolic microspheres, and the antibiotic composition Imipenem-Cilastatin (IMP-CS). However, permanent spheres are associated with more adverse events [3]

- The purpose of this study was to assess the safety and preliminary efficacy of SakuraBead in humans, a novel resorbable particle specifically designed for MSK embolotherapy, in the treatment of knee osteoarthritis.

Materials and Methods

- This prospective, single-arm, unblinded, first-in-human study was performed in 15 patients (13 women, mean age 62.8). Genicular artery embolisation (GAE) was performed with 200 µm SakuraBead resorbable microspheres. Patients were assessed with the Pain Visual Analogue Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline and at 1 and 3 month(s). Adverse events were recorded at all time points. This study was approved by the Ethics Committee of the Ministry of Health of the Republic of Uzbekistan, under Good Clinical Practice standards and the ethical principles of the Declaration of Helsinki.

- All patients had moderate KOA (Kellgren-Lawrence grade 2 or 3) and were asked to record their degree of pain using a 100-point VAS, together with pain, stiffness and disability evaluation using the WOMAC questionnaire (which rates pain 0-20; stiffness 0-8; and physical function 0-68), all at baseline, 1 and 3 month(s) post-procedure. The individual baseline information is given in Table 1.

- To inject Sakura beads, an Anterograde puncture of the ipsilateral common femoral artery was performed via a 5F sheath, a 1.7-2F microcatheter was used to cannulate the genicular arteries corresponding to the site of the patient's pain. SakuraBead was delivered in 0.2ml aliquots to prune the abnormal area of hyperaemia. Technical success was defined as the ability to catheterize and embolise the target genicular arteries.

Patient	Age	Gender	BMI (kg/m^2)	Knee Laterality	Kellgren-Lawrence Class	WOMAC Score Pain/Total	Baseline VAS Pain Score
1	61	F	35.9	R	2	8 / 48	60
2	62	M	30.4	R	3	9 / 38	60
3	78	F	28	R	3	14 / 47	80
4	52	F	23.6	L	3	15 / 57	80
5	65	F	32	R	3	16 / 66	75
6	60	F	39.1	R	2	16 / 55	70
7	76	F	30.5	R	3	14 / 58	70
8	59	F	25.2	L	3	15 / 58	80
9	60	F	33.7	L	2	13 / 61	80
10	72	F	29.4	R	3	10 / 61	90
11	51	F	29.7	L	2	8 / 27	60
12	49	F	30.4	L	2	14 / 52	80
13	74	M	25.3	R	3	10 / 57	80
14	53	F	24.2	R	2	15 / 58	90
15	70	M	26.4	R	2	11 / 51	80

BMI = body mass index; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = Visual Analogue Scale.

Table 1. Individual Patient Baseline Information

Baseline patient characteristics and treatment procedure

- Overall, 46 patients were screened for suitability to select the target number of 15 patients. All the treated patients showed characteristics of abnormal hypervascularity (Figure 1).
- The average volume of SakuraBead suspension injected to reach the desired embolisation endpoint was 1.1 ml (a range of 0.4-1.9 mL) which embolised an average number of 2.4 genicular arteries per patient. GAE was achieved in all the patients with 100% technical success.
- A total of 36 injections were performed across the 15 patients and the targeted locations of these injections in vascular anatomy are given in Figure 2.

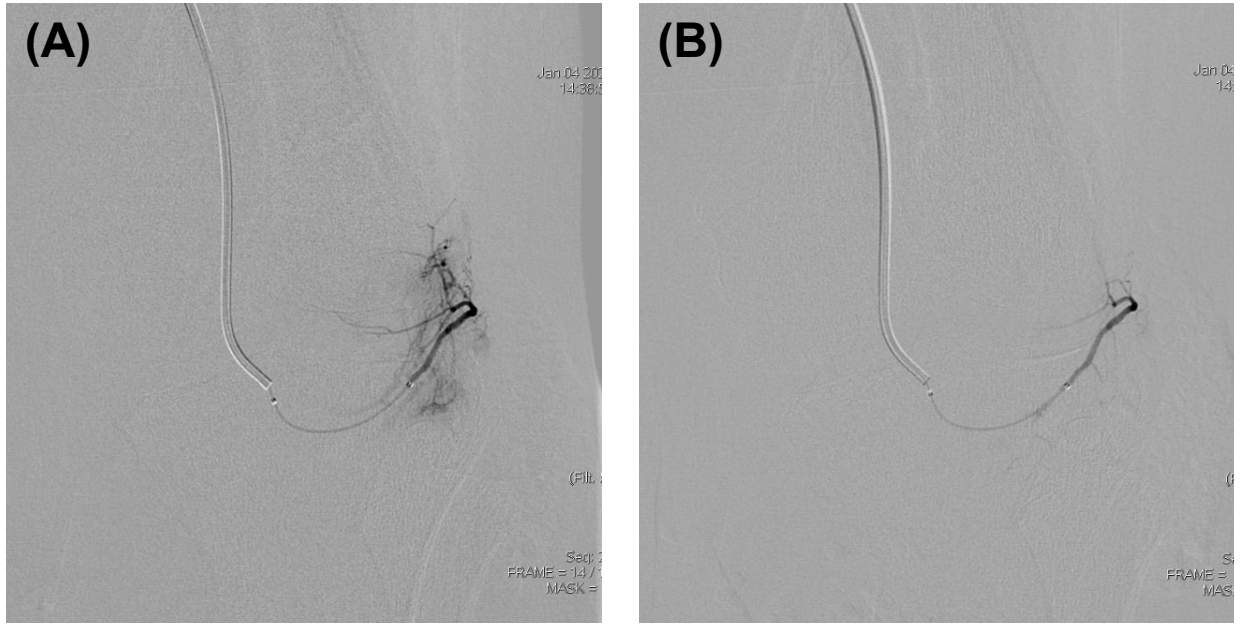

Figure 1: (A) A typical angiogram of the neo vessel blush seen in the inferior lateral genicular artery of one of the patient and (B) angiogram showing devascularisation of the blush following injection of 0.4mL
of embolic suspension

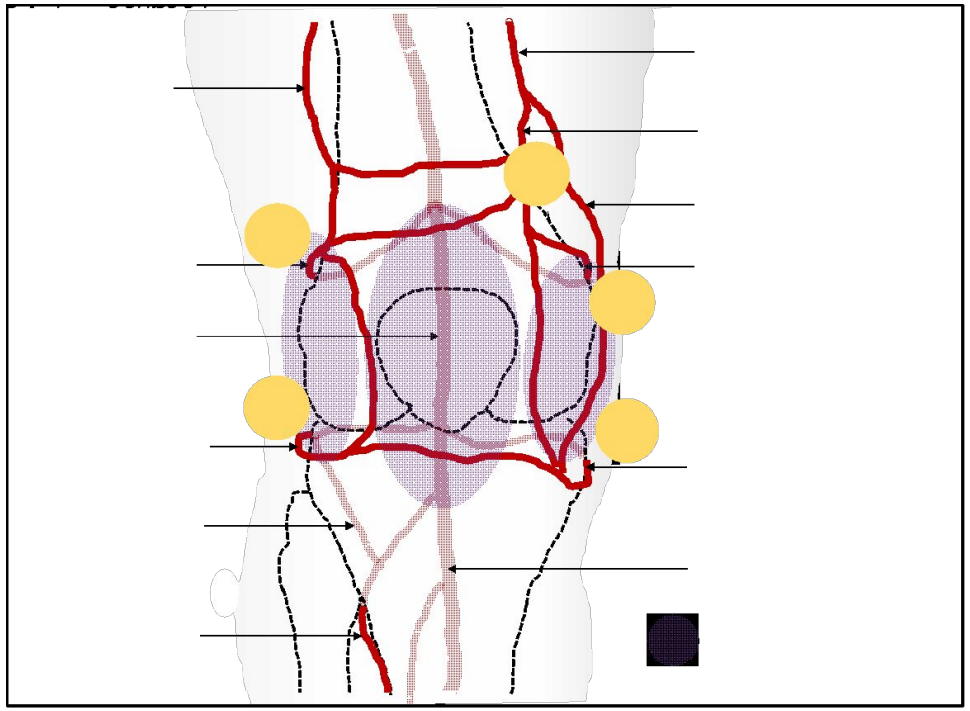

Figure 2: Vascular anatomy of the knee and targeted locations of the 36 injections performed across the 15 patients in the study

Primary performance outcomes

- 14/15 patients demonstrated significant improvement in VAS and WOMAC scores at 1 and 3-month(s) follow-up as shown in Figure 3. The mean pain VAS scores of treated patients compared to the baseline at 1 and 3-month follow-ups reduced significantly ($p < 0.001$) by 73.79% and 75.72% respectively. The statistical reduction in pain was maintained at 3 months despite one non-responder patient.

- A similar reduction in scores for WOMAC and WOMAC pain was observed. The total WOMAC scores were reduced significantly ($p < 0.001$) by 79.1% at 1 month and remained unchanged at 3 months. The WOMAC pain score was significantly reduced ($P < 0.001$) by 80.29% at 1 month with further reduced to 82.44% from baseline at 3 months.

- The subcategory of WOMAC pain score was also reduced for pain (80.29%), stiffness (77.92%) and physical function (78.81%).

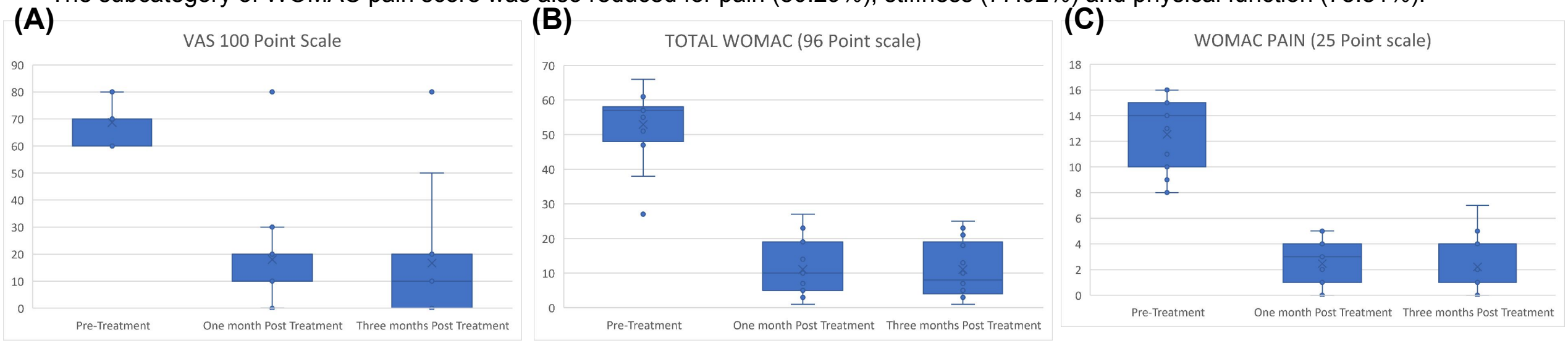

Figure 3: (A) VAS Pain score; (B) WOMAC Total score and (C) WOMAC 20-point functional scale

Conclusions

1) This study supports the safety and efficacy of GAE for reduction of knee pain secondary to KOA.
2) The Primary Performance Endpoint of this clinical investigation was achieved in 14/15 (93%) of patients.
3) The results for Pain VAS and WOMAC questionnaire scores demonstrate that treatment using SakuraBead provided a statistically significant improvement in pain, stiffness and physical function for patients
4) Adverse events were all mild and transient in nature
5) The clinical investigation provides robust evidence that SakuraBead Resorbable Microspheres are a safe and effective option for Genicular Arterial Embolisation to treat pain secondary to knee osteo-arthritis.

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