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## Catastrophic failure of cup revision hip arthroplasty due to undiagnosed Paget disease of bone: A case report

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## ABSTRACT

**INTRODUCTION:** Paget's disease of bone (PDB) is a localized chronic osteopathy, apparently not genetic in origin, and frequently diagnosed from incidental radiographic images. The disease is characterized by deformation, hypervascularity, and structural weakness of the bone and by changes in joint biomechanics. Most cases of PDB can be easily diagnosed from radiographic findings, but monostotic cases may be problematic and require invasive procedures.

**PRESENTATION OF CASE:** A 70-year-old woman had re-revision surgery for early catastrophic failure of an isolated cup revision hip arthroplasty because of undiagnosed PDB 21 years after the primary total hip arthroplasty. To identify the pathomechanism of early failure, we performed bone biopsy on the right iliac crest. Histopathological findings showed a mosaic pattern in the bone characteristic of PDB. Prior to the planned re-revision surgery, we treated the PDB with denosumab until the patient's serum level of alkaline phosphatase (ALP) was within the normal limits. Two months after denosumab treatment, we performed re-revision hip arthroplasty using a structural allograft and a Kerboul-type reinforcement device.

**DISCUSSION:** The delay in correct diagnosis of PDB was associated with the rapid destruction of pelvic bone. The preoperative use of antipagetic medication could decrease the risk of implant loosening and may be warranted to mitigate that risk.

**CONCLUSION:** In patients with a failed arthroplasty, thoughtful evaluation is warranted for preoperative antipagetic medication in order to reduce PDB activity and potentially decrease the risk of implant loosening. This paper offers some steps for such risk reduction in the workup before revision surgery.

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## 1. Introduction

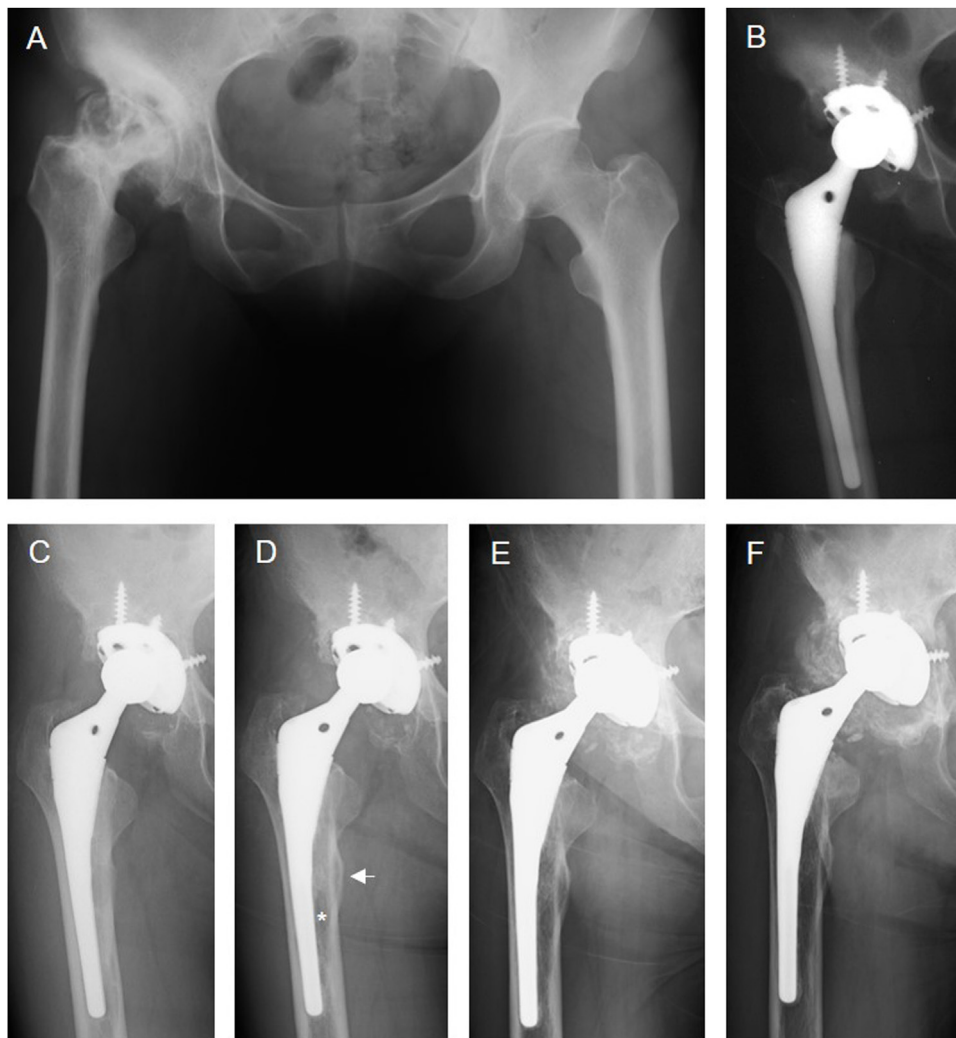
Paget's disease of bone (PDB) is commonly associated with focal abnormalities of bone remodeling at one or more sites. Named for Sir James Paget, who described it in 1877, PDB is currently considered a localized chronic osteopathy that results in increased bone resorption, followed by the formation of new bone containing microstructural defects. PDB can affect a wide range of bone types, but is most common in the axial skeleton; 67% of cases manifest in the pelvis, 39% in the spine, 33% in the femur, 19% in the tibia, and 25% in the skull [1]. Bone pain, the most common symptom, tends to be constant, including at rest, and to worsen at night [2]. Other symptoms may include stress fractures, bony enlargement, gait disturbance, and secondary osteoarthritis. Diagnosis is often

based on incidental radiographic findings or elevated serum alkaline phosphatase. Here we report a case of a 70-year-old woman who had re-revision surgery for early catastrophic failure of an isolated cup revision arthroplasty, due to undiagnosed PDB, 21 years after primary total hip arthroplasty. The patient died before this case report was completed, so the next of kin provided informed consent regarding the submission of case data for publication. This work has been reported in line with the SCARE criteria [3].

## 2. Case presentation

A 70-year-old Asian woman presented to our hospital with right hip pain. Her past medical history included renal sclerosis treated with hemodialysis for 15 years, a dissecting aortic aneurysm (DAA) for which she was treated conservatively, and osteoarthritis secondary to developmental dysplasia of the hip, which was treated with a total hip arthroplasty (THA) when she was 48 years old (Fig. 1A,B). The patient was temporarily lost to follow-up but started annual check-ups at our out-patient clinic ten years after the THA

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**Fig. 1.** (A) Anteroposterior (AP) radiograph of the pelvis obtained before a primary THA. (B) Postoperative AP radiograph obtained immediately after primary THA using cementless implants. (C) Postoperative AP radiograph obtained 14 years after surgery. No remarkable changes were noted compared with the radiograph immediately after surgery. (D) Postoperative AP radiograph obtained 19 years after surgery. Although the acetabular side was almost the same as in (C), atrophic changes in the medullary canal (asterisk) and focal ballooning of the cortical bone (white arrow) were noted in the femur at the level of the middle part of the stem. (E) Postoperative AP radiograph obtained 20 years after surgery. Change in the femoral side was more noticeable, and patchy opacity became visible around the cup. (F) Postoperative AP radiograph obtained 21 years after the surgery. The patchy opacity around the cup has the cotton wool appearance characteristic of PDB.

(Fig. 1C). Despite an initially promising postoperative recovery, she complained of new pain in her right thigh during her regular 14-year postoperative check-up after the surgery. The cause of her pain was not diagnosed at that time. Due to the risks associated with her DAA, she was monitored and treated conservatively with painkillers.

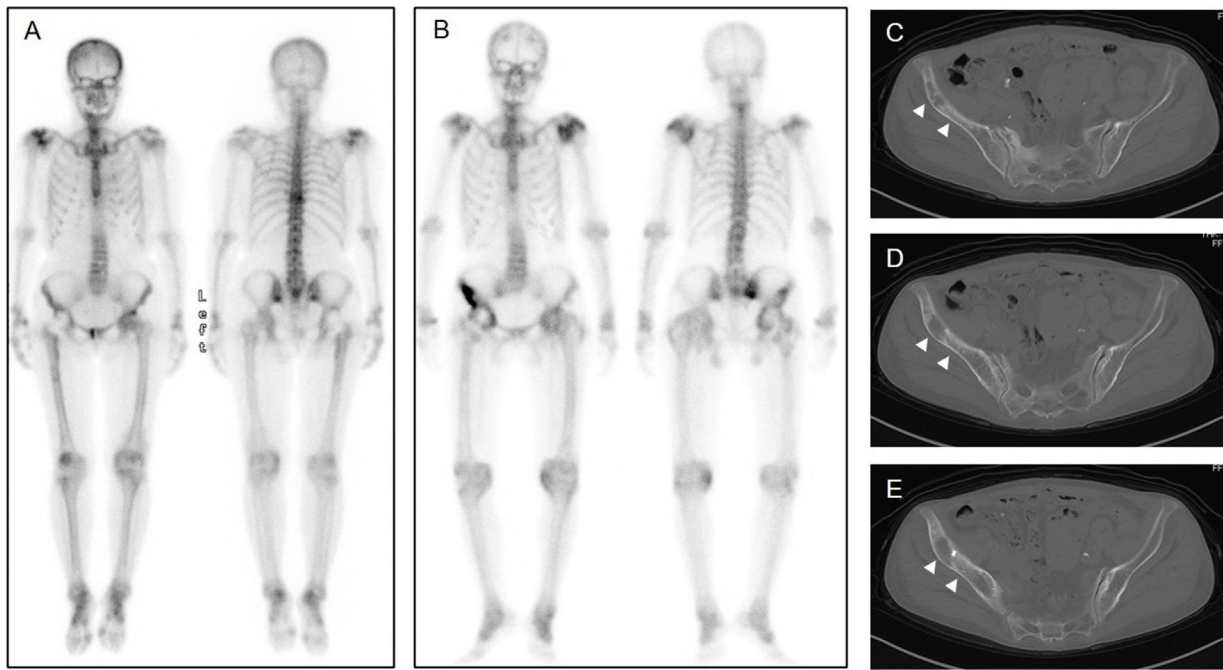
She complained of right leg pain again at her 19-year postoperative annual check-up, but an anteroposterior (AP) pelvic radiograph showed no change from her 14-year check-up (Fig. 1D). She was diagnosed with lumbosacral radiculopathy and underwent L4/5 posterior lumbar interbody fusion, which improved the right leg pain.

At her 20-year postoperative check-up, an AP pelvic radiograph showed an expanded mixed osteolytic and osteosclerotic lesion around the neck of the femoral stem (Fig. 1E). At the 21-year postoperative check-up, an AP pelvic radiograph showed further extension of the lesion (Fig. 1F). The patient complained of chronic right groin pain, although the right leg pain had improved after the lumbar fusion. At that check-up, her laboratory tests showed slightly elevated alkaline phosphatase (ALP) activity (386 U/L; reference range: 115–359 U/L), C-reactive protein (0.88 mg/dL)

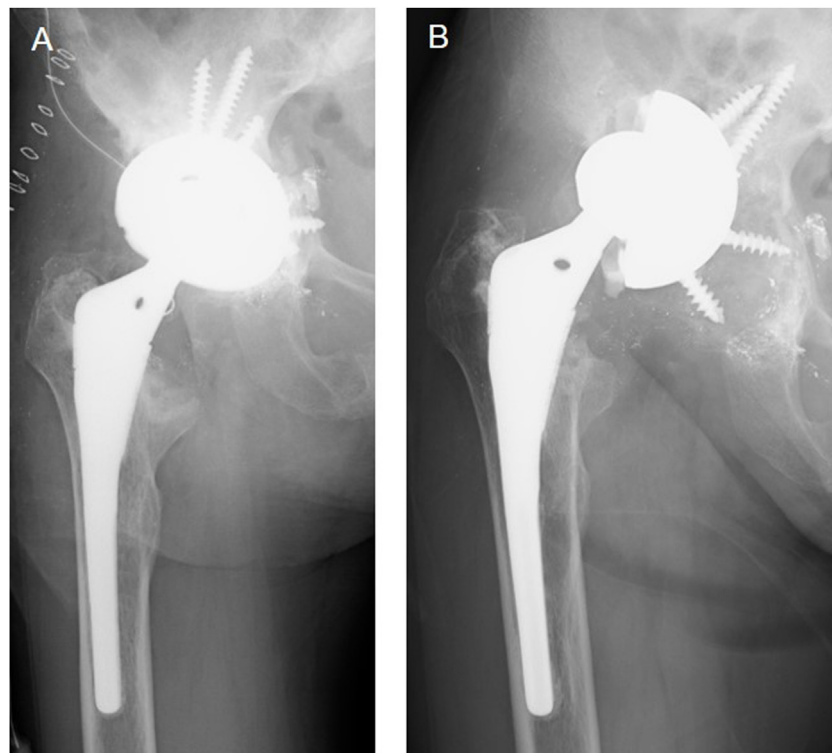
and erythrocyte sedimentation rate (34 mm/h). Her white blood cell count was normal (5780 cells/ $\mu$ L). Technetium-99 m bone scintigraphy showed focal areas of increased activity in the anterior part of the right iliac wing that had not been noted 6 years previously (Fig. 2A,B), and computed tomography (CT) showed mixed osteosclerotic and osteolytic changes in the right iliac wing (Fig. 2C–E). Of interest, although unnoticed when evaluating the patient for the first cup revision arthroplasty, increased activity in the skull was seen on the bone scan taken 14 years after the primary THA (Fig. 2A). Considering these findings, we speculated that the lesion was due to an aseptic cup, which was loosening because of the rigidity of her lumbar spine due to the L4/5 PLIF, and we elected to perform an isolated cup revision arthroplasty.

A cementless jumbo cup (Zimmer 56-mm Trabecular cup) was implanted with a 32-mm cobalt-chromium femoral head and a highly cross-linked polyethylene liner (Fig. 3A). During the surgery, we noted fluid collection in the articular space, but a Gram stain showed no white blood cells or organisms, and no growth was noted after fourteen days of culture.

Unexpectedly, the jumbo cup dislodged 14 months after the revision surgery, making it difficult for the patient to walk. A



**Fig. 2.** (A) Bone scintigraphy obtained 14 years after the primary THA showed slight bone tracer accumulation in the right proximal femur but no obvious accumulation in the anterior pelvic wing or around the cup. Increased activity was noted in the skull. (B) Bone scintigraphy obtained 20 years after the primary THA showed considerable accumulation in the anterior pelvic wing, more than in the circumference of the cup. (C–E) Computed tomography showing mixed osteosclerotic and osteolytic changes in the right iliac wing (arrowheads).



**Fig. 3.** (A) Postoperative AP radiograph obtained immediately after revision arthroplasty using a jumbo trabecular cup. (B) Postoperative AP radiograph obtained one year after revision arthroplasty with the jumbo trabecular cup, showing obvious dislodgement of the cup.

bone biopsy from the right iliac crest was performed under local anesthesia to identify the pathomechanism of this early failure. The histological findings on biopsy showed no evidence of amyloid deposition or malignant cells. However, a mosaic pattern with thick cement lines demarcated randomly oriented lamel-

lar bone, a pathognomonic histologic finding of Paget's disease (Fig. 4).

We reevaluated the x-ray obtained 21 years after the initial THA and recognized that the rapid-onset atypical osteolytic change around the cup without severe polyethylene wear showed a cot-



**Fig. 4.** Histologically, thick cement lines were noted that demarcate randomly oriented lamellar bone characterized as a mosaic pattern, indicating a mix of findings compatible with PDB. (Hematoxylin and eosin stain).

ton wool appearance characteristic of PDB (Fig. 1F). We deduced that increased activity in the pelvic wing rather than at the circumference of the cup on preoperative bone scan was unlikely to be caused by the loosening of the cup. We concluded that the new onset of PDB caused the early failure of the isolated cup revision arthroplasty.

We hypothesized that PDB was also the cause of the initial right thigh pain, since that bone pain was consistent with PDB. In retrospect, on the bone scan taken 14 years after the initial THA, we should have recognized the increased tracer accumulation in the skull as a sign of PDB.

Because of the severity of the acetabular bone defect, we prepared a 3D-printed model of this patient's acetabulum when planning the re-revision (Fig. 5A,B). Before the planned re-revision surgery, the patient was treated with denosumab until her ALP level was within the normal limits (WNL), which took two months. At that point, her serum C-reactive protein, calcium, and phosphate were also WNL. We removed the trabecular cup and reconstructed the acetabulum, which had severe bone deficiency, by using a structural allograft and a Kerboull-type reinforcement device (Fig. 5C–E).

Postoperatively, the patient started walking after 6 weeks and experienced minimal discomfort at one-third partial weight-bearing. By three months, she had returned to her baseline ambulatory status. At the 6-month follow-up, radiographs showed no evidence of implant loosening, subsidence, or fracture on radiographs, and she was able to walk without any discomfort. Her ALP remained WNL, Harris hip score totaled 81 points, and the self-administered Japanese Orthopaedic Association Hip Disease Evaluation Questionnaire (JHEQ) was scored at 56 out of 84 points [4]. Unfortunately, four months after the final follow-up the patient died suddenly from heat shock while bathing. It was determined that the cause of death was not related to her artificial right hip. Her next of kin told us that she maintained nearly normal ambulatory status until her death.

### 3. Discussion

To our knowledge, this is the first report documenting a case of undiagnosed Paget disease of bone causing an acetabular cup

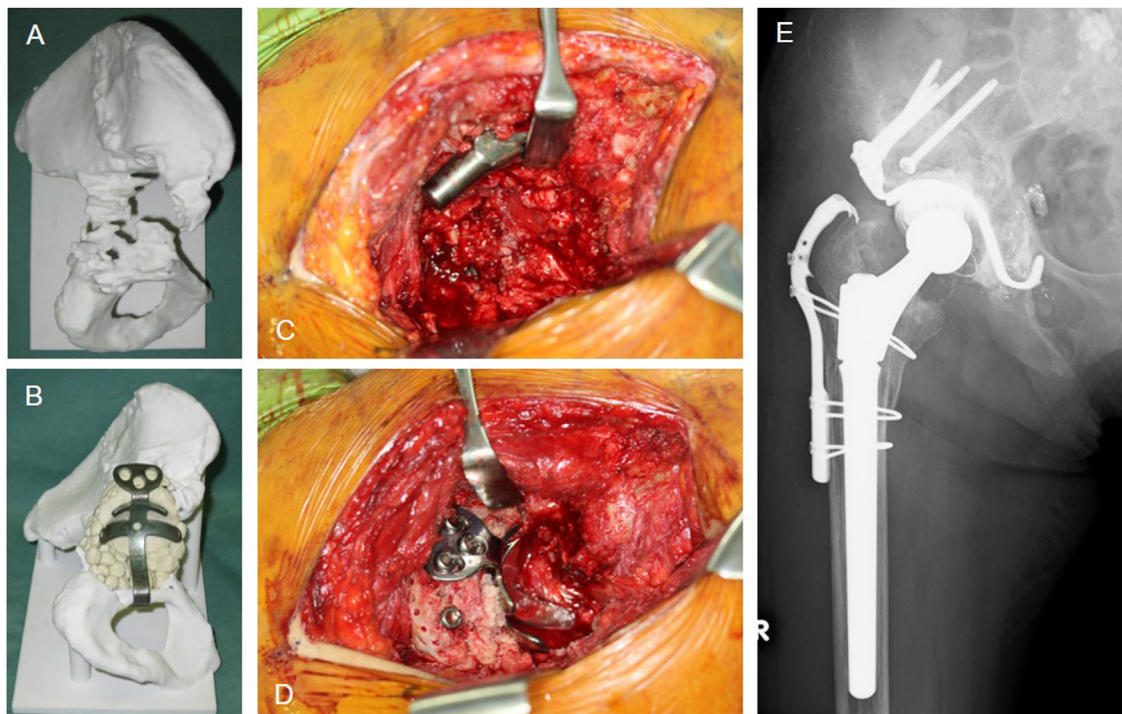
to loosen 21 years after the primary THA, and causing the early dislodgement of an acetabular cup after an isolated cup revision arthroplasty.

As shown in this case, when a re-revision arthroplasty procedure is necessary, a full workup is required. The workup should include all necessary imaging and a bone scan to determine whether the loosening of the implant is due to bone destruction or to a neoplastic process. In our case, serial X-rays were useful in diagnosing PDB. If PDB is suspected, the patient should be referred to an endocrinologist, and metabolic bone disease should be ruled out. The patient should be fully informed of the benefits and risks of re-revision surgery and PDB when deciding whether to pursue the option of surgery.

Caucasian men over 55 years of age have a 2% incidence of PDB. The cause is currently unknown and may involve both predisposing genetic factors and environmental factors [5–7]. Histologic findings of bone marrow fibrosis and woven bone are seen in many bone turnover conditions including metabolic disorders, and are thus not pathognomonic for PDB [8]. When PDB is confirmed, bisphosphonate treatment before surgery will maximize the chance of a successful fixation.

Promising results have been recorded with uncemented components in PDB; studies have shown positive mid-term outcomes and fixations [9–12]. However, the use of uncemented components may be less beneficial in patients with active PDB, which may compromise fixation, causing bone to grow into cementless implants.

Interestingly, studies have demonstrated that fractures can heal as successfully in patients with PDB as in healthy individuals [13]. Wegrzyn et al. reported that PDB patients with elevated ALP have a significantly higher incidence of implant loosening than patients with ALP WNL. For this reason, preoperative antipagetic medication, such as bisphosphonates, is necessary to reduce disease activity and insure a good outcome of cementless THAs [14]. Antipagetic medication has been shown to aid in bone healing. Bisphosphonates increase the cellular response in mature and healing bone, and in pre-clinical trials zoledronic acid has enhanced bone growth into porous implants [15,16]. Unfortunately, bisphosphonates are contraindicated in patients with kidney disease with low glomerular filtration rate (GFR) or dialysis status due to the risk of



**Fig. 5.** (A) A 3D-printed acetabular model generated using computed tomographic data from the patient. Notable bone defects in the acetabulum were noted, although bone deficiency had not yet led to pelvic discontinuity. (B) Preoperative planning for acetabular reconstruction using a crouton-size allograft and molded half femoral head allograft with a Kerboull-type reinforcement device. (C) Intraoperative photos showed severe bone deficiency in the acetabulum. (D) The acetabulum was reconstructed successfully by using a structural allograft and a Kerboull-type reinforcement device. (E) Postoperative AP radiograph obtained immediately after the re-revision arthroplasty.

further kidney injury or severe hypocalcemia. For those patients, less effective treatments are recommended. Schwarz et al. reported that patients with PDB and severely low GFR who were treated with denosumab showed rapid decreases in bone remodeling as evaluated biochemically and by bone scintigraphy [17]. Based on the outcomes described by Schwartz et al., we selected denosumab rather than bisphosphonates for antipagetic presurgical treatment in this patient. Fortunately, the denosumab treatment was rapidly effective, and the patient reported outcome measures at the last follow-up were satisfactory. Due to her untimely death, it was impossible to determine the long-term stability of the implant.

#### 4. Conclusion

The correct diagnosis of Paget disease of bone was delayed and resulted in rapid destruction of the pelvic bone. Going forward, we recommend determining serum ALP levels before performing invasive procedures in older patients with suspicious bone lesions. We also encourage consideration of the use of antipagetic medication before orthopedic surgery to reduce the risk of bone destruction. Paget's disease of the bone, although rare in Asian populations, may contribute to the loosening of arthroplasty components. The situation of our patient emphasizes the importance of an appropriate workup prior to surgery, both to rule out other conditions and also to develop an appropriate operative plan if revision surgery is undertaken.

#### Declaration of Competing Interest

The authors report no declarations of interest.

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None.

#### Ethical approval

Case reports are exempt from the need of IRB approval in our institute.

#### Consent

Written informed consent was obtained from the next of kin for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contribution

**Conceptualization, Writing of manuscript, Literature review:** Kiyokazu Fukui.

**Data collections:** Kiyokazu Fukui, Katsutaka Yonezawa, Akihiro Shioya.

**Data analysis:** Kiyokazu Fukui, Akihiro Shioya.

**Reviewing of the final version of the manuscript:** Kiyokazu Fukui, Ayumi Kaneuji, Toru Ichiseki, Norio Kawahara.

#### Registration of research studies

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#### Guarantor

Kiyokazu Fukui.

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