

## Supplementary Appendix

Supplement to: Xue F, Wang P, Yuan Z, et al. Total knee arthroplasty after gene therapy for hemophilia B. *N Engl J Med* 2022;387:1622-3. DOI: 10.1056/NEJMc2211173

This appendix has been provided by the authors to give readers additional information about the work.

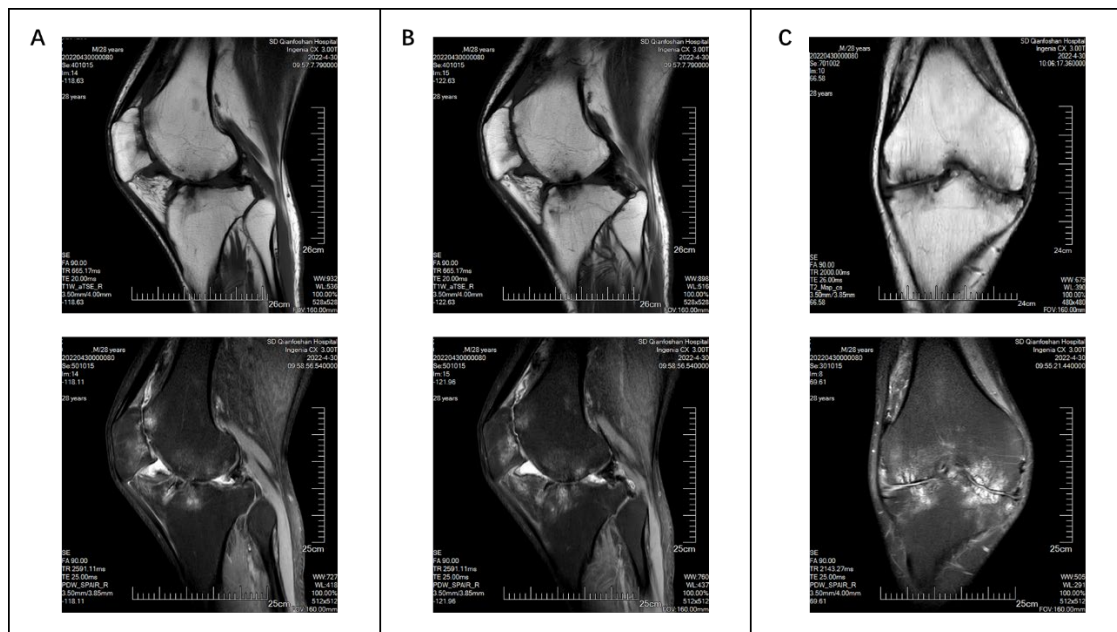
# Supplementary Material

## Total knee arthroplasty after gene therapy for haemophilia B

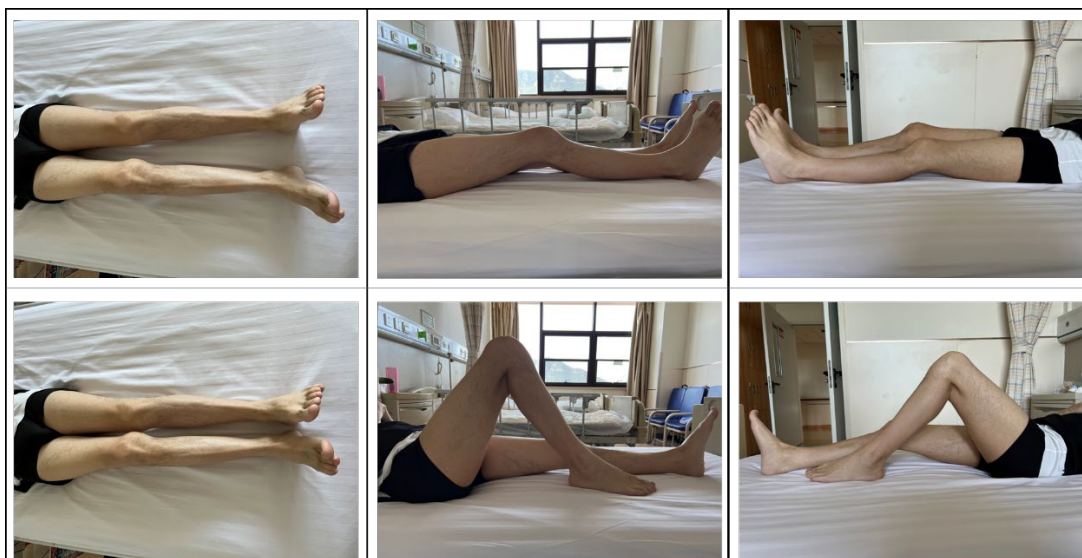
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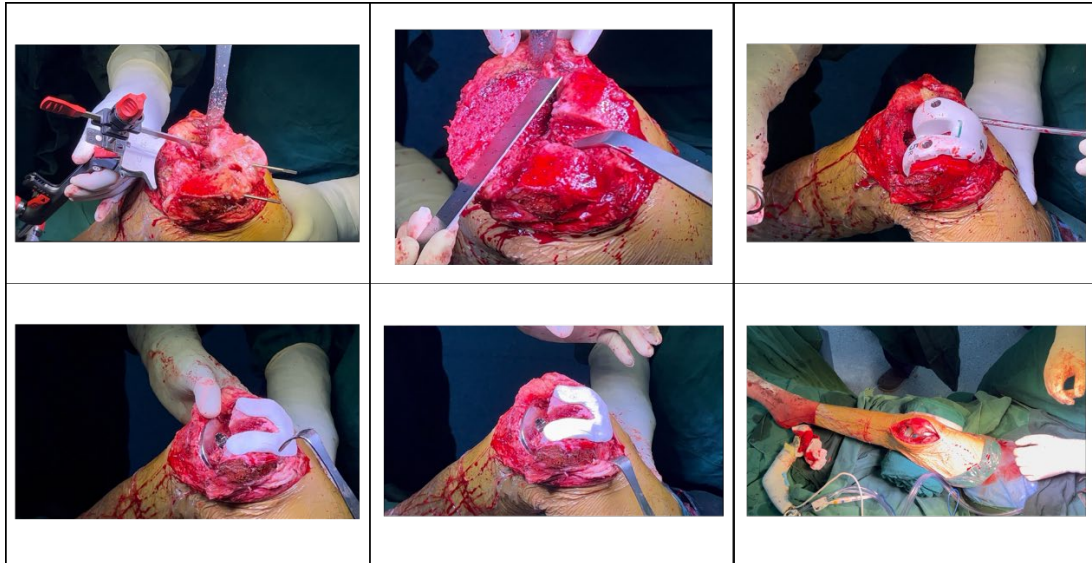
## 1. Supplementary Figures



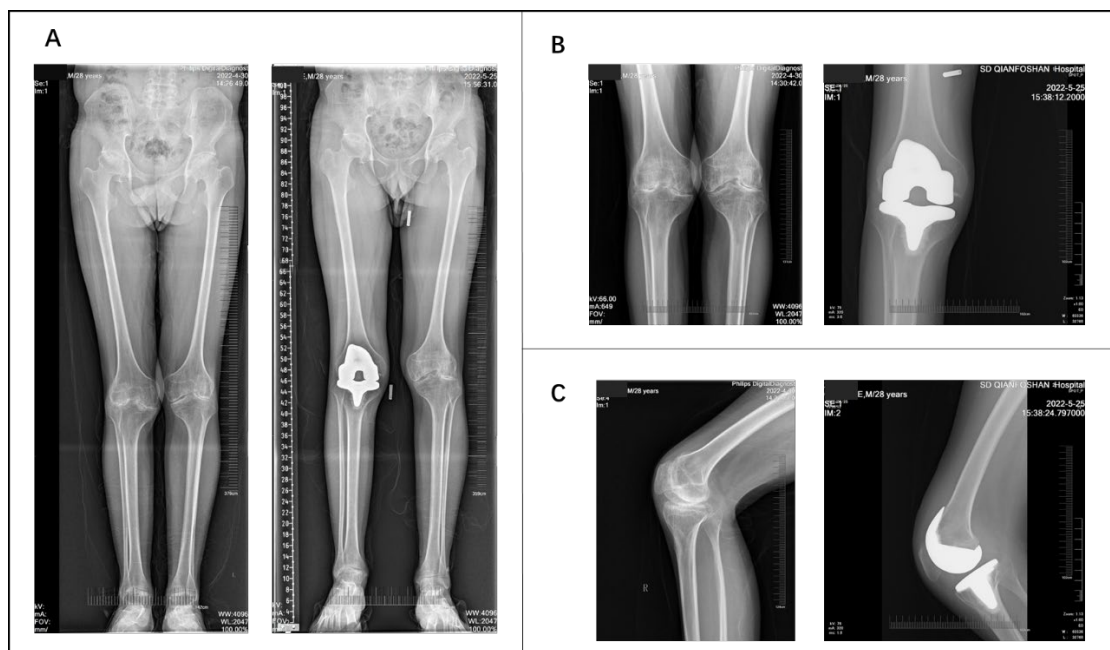
**Figure S1. MRI of the right knee joint before the TKA operation.** Panels A and B show the articular cartilage of the right knee is narrowed and disappeared to varying degrees, bone marrow edema and cystic degeneration under the articular surface; deformation and damage of the infrapatellar fat pad; and formation of suprapatellar synovial folds. Panel C shows the structure of the meniscus disappears; the articular cartilage is narrowed and disappeared to varying degrees, the joint space is significantly narrowed, and the articular surface bone has multiple edema and cystic degeneration. These findings are consistent with haemophilic arthropathy.



**Figure S2. Morphology of both knee joints before the TKA operation.** These photos show the morphology, and range of motion of both knee joints before the TKA operation.



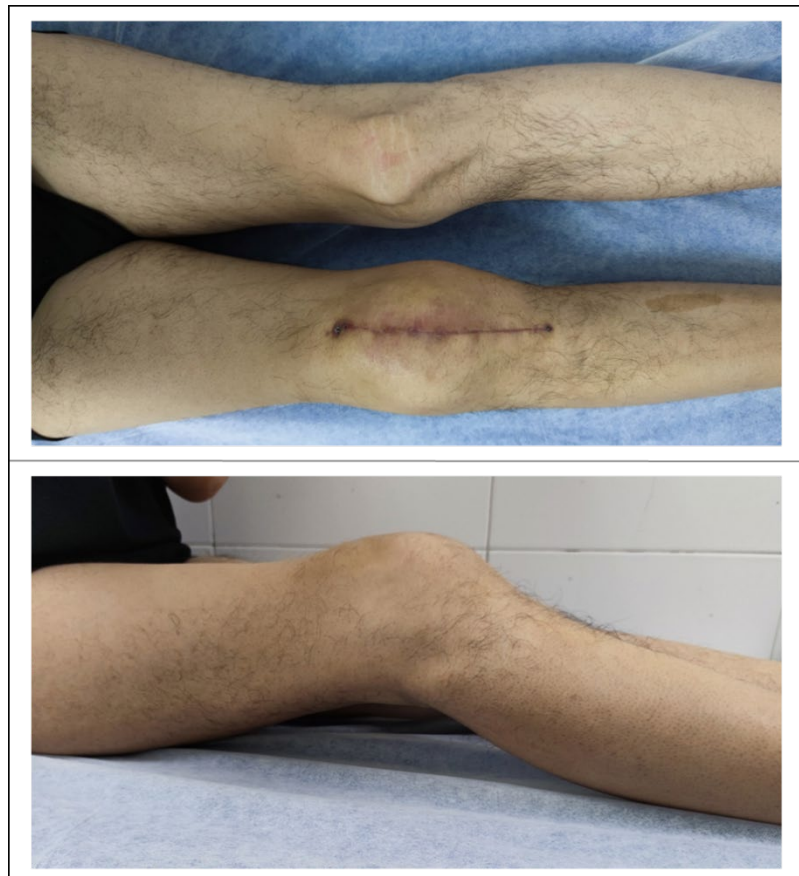
**Figure S3. The bleeding situation during the TKA operation.** These photos show the process of the TKA operation. No excess uncontrol bleeding happened and the intraoperative blood loss was estimated at 150 mL.



**Figure S4. Anteroposterior & lateral X-rays of the right knee joint of this HB patient before and after the TKA operation.** The left graphs of panels A, B, and C are X-rays of this patient before the TKA operation, which show the bone end of the right knee joint is enlarged and osteophytes are formed; the joint space is narrowed, the articular surface is uneven with bone sclerosis, and scattered low-density cystic degeneration areas under the articular surface. These findings are consistent with haemophilic arthropathy. The right graphs of panels A, B, and C are X-rays of this patient after the TKA operation, which show after TKA of the right knee joint, the fixation is well aligned and fits well with the surrounding tissues, and there is no obvious sign of loosening.



**Figure S5. Right knee on day 1 after the TKA operation.** This photo was taken on day 1 after the TKA operation which shows the clean surgical wound with no obvious bleeding and swelling.



**Figure S6. Morphology of right knee 42 days after the TKA operation.** This photo was taken on 42 days after the TKA operation which shows the surgical wound healed well with no infection.

## 2. Supplementary Tables

**Table S1.** HEAD-US-C score<sup>1</sup> of this HB patient

Date	Elbows		Knees		Ankles		Total
	Left	Right	Left	Right	Left	Right	
2016/09	8	6	6	6	1	4	31
2021/01	8	6	5	6	2	8	35
2022/01	10	6	7	8	3	9	43

**Table S2.** FIX:C measured with two assays and thromboelastography (TEG) during the perioperative period of TKA.

	Factor IX activity level (IU/dl)		R (min)	Angle (°)	K (min)	MA (mm)
	Actin FSL	Actin	NR: 5-10	NR: 53-72	NR:1-3	NR: 52-70
D0 before	50.1	92.6	6.9	49.5	3.2	52.5
D0 after	46	77.9	6.9	49.5	3.2	52.5
D1	53.8	89.8	ND	ND	ND	ND
D2	57.9	91.9	ND	ND	ND	ND
D3	67.1	97.2	ND	ND	ND	ND
D4	75.7	104.6	ND	ND	ND	ND
D5	79.3	108.1	ND	ND	ND	ND
D6	73.4	103.7	ND	ND	ND	ND
D7	75.7	112.7	ND	ND	ND	ND
D8	67.1	112.7	ND	ND	ND	ND
D9	68.1	113.6	ND	ND	ND	ND
D10	61.4	100.4	ND	ND	ND	ND
D11	60.5	98	ND	ND	ND	ND
D12	64.1	102.9	ND	ND	ND	ND
D13	62.3	98.8	ND	ND	ND	ND
D14	62.3	98.8	ND	ND	ND	ND

\* R: reaction time; Angle: kinetics of clot development; K: kinetics time; MA: maximum amplitude; NR: normal range; ND: not done.

## 3. Reference

1. Dou X, Poon MC, Yang R. Haemophilia care in China: Achievements in the past decade. *Haemophilia*. 2020;26(5):759-767.