Joint received 50 uL of saline. Injections into each joint cavity were achieved by inserting the needle point just below the patella after incision of the skin to reveal the joint. Both for sensitization and i.a. mBSA injection, and for MRI, rats were anesthetized with isoflurane (Rothacher-medical) 1.5–3% in an air/oxygen mixture.

Four sites (two on the back and one on each forepaw) with 100uL antigen solution (500 ug methylated bovine serum albumin (mBSA, Sigma-Aldrich)/50 uL saline plus 50 uL complete Freund’s adjuvant (Becton Dickinson)). At the same time, animals received an intraperitoneal injection of 2x10^9 heat-inactivated Bordetella pertussis (Institut Pasteur - Paris). The sensitization procedure was repeated after 7 days (D-14) by an intradermal injection at four sites on the back. Mono-arthritis was induced 14 days later (D0) in the sensitized animals. The right knee joint was challenged by an intra-articular (i.a.) injection of 500ug mBSA in 50uL saline, while the left knee joint received 50 uL of saline. Injections into each joint cavity were achieved by inserting the needle point just below the patella after incision of the skin to reveal the joint. Both for sensitization and i.a. mBSA injection, and for MRI, rats were anesthetized with isoflurane (Rothacher-medical) 1.5–3% in an air/oxygen mixture.

Scanning was carried out on a Siemens MAGNETOM Trio, a Tim system, 3T clinical scanner (Siemens AG, Erlangen, Germany) using the system 4cm loop coil. Time points were a pre scan before the model was started (day -21), a baseline scan after immunization, but before induction (day 0) followed by simultaneous scanning of the diseased knee and the contra lateral control joint at days 3, 6, 10, 13 and 17. The protocol parameters included T2 STIR 2D for oedema, TR/TE 3700/20ms, Flip angle 150°, Resolution 0.31mm FOV 100mm. Anaesthetized animals were monitored with a respiratory pad, and ethical committee approval was obtained for the complete protocol. Histological staining (HE) was carried out on animals sacrificed at each time point. Statistical analysis of data included exponential fits of the development of each component of the disease and comparison of the derivative coefficients by Friedman non-parametric comparison and by Wilcoxon for the placement of the time of maximum score.

Images showing the disease progression are shown in figure 1. Scoring shows the development and diminution of oedema over the timescale of the imaging.

Scoring of oedema types and bone erosion mean ± SEM with double exponential fit of rise and decay (d0 n=24, n-3 at each time, fit R²> 0.8)

Corresponding histology slices at days 3 and 17 from different animals showing oedema swelling and bone loss.

All left control knees scored zero for oedema and bone erosion, unlike diseased right knees that showed the rapid development of a synovitis with periarticular oedema, followed by bone erosion and joint effusion. Slight intra-bone oedema appears at day 6 and remains constant for the time period studied. Figure 2 shows fitting of mean scores with time and SEM shows consistency between animals. R² also shows good fits for the data from the individual animals (0.60 to 0.94). Comparing the position of the maximum (max) of a double exponential fit of the data for individual animals with images at all time points, the Wilcoxon analysis shows a significant difference (p=0.043) for the time to peak of extra-articular oedema and intra-articular oedema. Fits for erosion did not produce maxima and continued to grow outside the timescale studied, however, the exponential coefficients from the fit produce a p<0.007 when compared by Friedman test between erosion and oedema. Correlation is seen between the scores on MR images and the corresponding histology (Figure 3).

Discussion and Conclusions
A robust and predictable AIA model in rat has been developed that is easily characterized by T2 STIR imaging. The progression of the different disease components can be tracked on MR imaging over time. The left knee that does not have the induced disease acts as an internal control throughout the serial study. Further serial treatment and progression studies can now be based on this well-defined model.