Introduction
Knee Osteoarthritis (OA) is a common musculoskeletal disorder in the United States that frequently causes disability [1-2]. Its progression is typically assessed with the Kellgren-Lawrence (KL) scale, a 0-4 scale in which higher scores imply more advanced OA [3]. When diagnosed early (KL = 0, 1), nonsurgical treatments such as exercise, weight loss, and injections can slow OA progression, but at late stages (KL = 4), no noninvasive option exists, making total knee replacement (TKR) the only option [4-5]. The procedure is effective but imperfect: only 66% of patients report their knees feeling “normal,” and 33% report pain post-implant [6]. This, as well as potential complications that necessitate revisions, makes delaying TKR preferable whenever possible [7-8]. Thus, a model predicting if patients will undergo TKR with high sensitivity and specificity would have utility, particularly at early-stage OA.

Methods
3D Double Echo Steady-State MRI images from the Osteoarthritis Initiative (OAI) were center-cropped to a 120×320×320 region, normalized, and converted to 14-bit [9]. Cases were defined as patients who underwent a first TKR within 5 years of an image; controls were patients who did not undergo a first TKR within 5 years and for whom another image was taken 5 years after the given image.

A scheme of the modeling pipeline used is shown in Figure 1a. A DenseNet-121 classifier was pretrained to predict OA from MRI images and fine-tuned to predict TKR. Image-based predictions were fed to one of three logistic regression (LR) ensembles based on OA severity, yielding a final prediction. Ensembles integrated image-based predictions with 21 non-imaging variables relevant to TKR, covering pain metrics, physical performance tests, and demographics [10-12]. Performance of 2 ensemble versions are reported: one where non-imaging variables were used to predict TKR (patient only), and one where image-based predictions were added (combined). DenseNet-121 output is also reported (image only). 75% of test cases were randomly sampled 100 times to calculate mean, standard error, and confidence intervals. Occlusion maps were developed for true positives, and anatomic regions with pixels among the top 5% of TKR probability change were designated as hotspots.

Results
Pipeline performance is shown in Table 1 and Figure 1b. Furthermore, areas under the Receiver-Operating Characteristic (ROC) curve are as follows, p < 0.01: 0.885 ± 0.021 (image only), 0.587 ± 0.042 (patient only), 0.830 ± 0.033 (combined).

Figure 1c is an example occlusion map. The following were hotspots in at least 83% of true positives: medial patellar retinaculum (MPR), synovium, tibiofemoral joint cartilage and bone (medial and lateral), anterior and posterior meniscus (medial and lateral), and Hoffa fat pad. All but the MPR are implicated in OA progression [13].

Conclusions
We present a pipeline that predicts TKR with strong sensitivity and specificity, particularly for less advanced OA. From occlusion map analysis, we find many tissues from which the pipeline drew most consistently to predict TKR have been implicated as OA biomarkers, which is logical, as TKR is an outcome of OA progression. This finding shows promise that further studies can facilitate discovery of additional imaging biomarkers, including those preferentially affecting TKR prediction probability for patients with no or moderate OA.

Highlights: We present a deep learning pipeline that uses 3D DESS MRI images and 21 non-imaging variables to predict TKR with high sensitivity and specificity, particularly for patients with less-advanced OA. The model may have utility in identifying an at-risk population so nonsurgical treatments can be implemented that delay TKR onset.

References