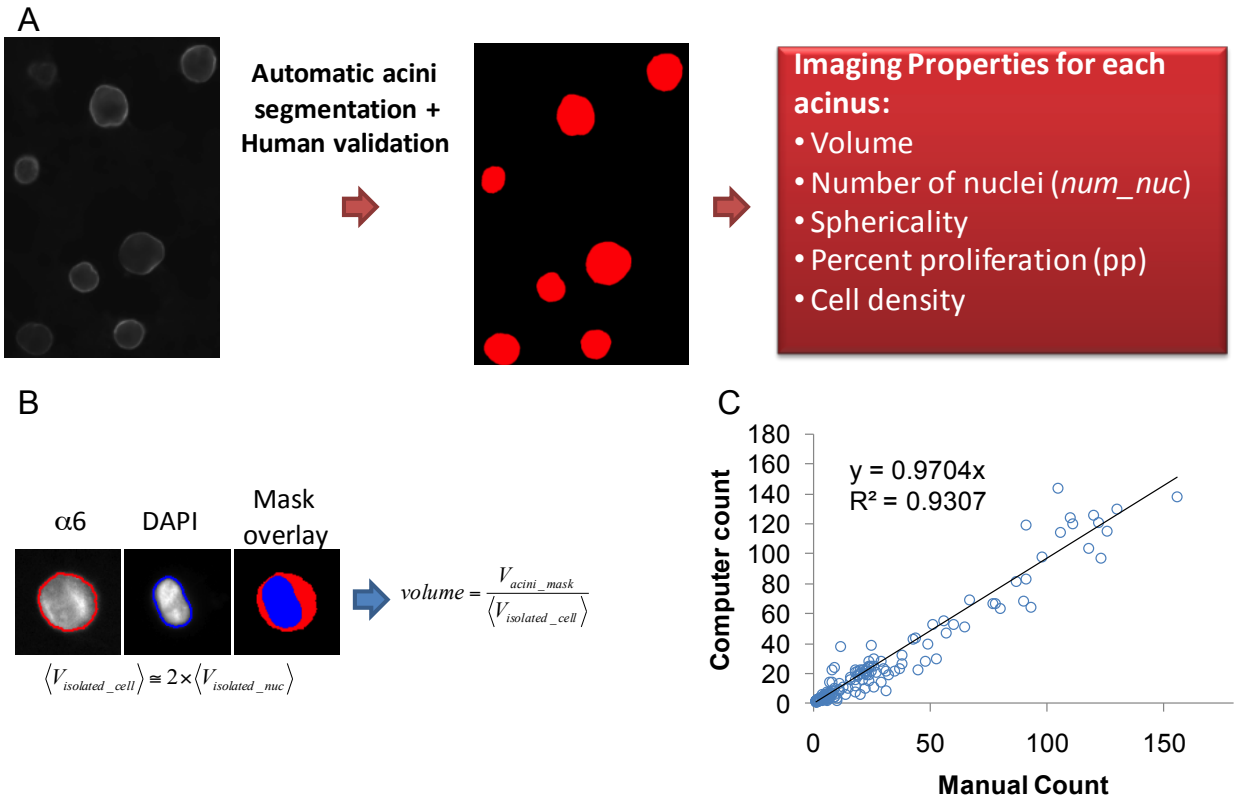

Fig. S1. Additional information on image analysis. (A) Imaging workflow: all image analysis are performed on 3D stacks with 5 μm step. To facilitate illustration, only the center slice is shown. The basement membrane marker α6 is used to segment individual acini, using automatic isodata thresholding. Any poorly segmented acini are manually removed. Once isolated, a list of imaging properties are automatically generated and tabulated based on the age and the type of culture. (B) Single cell quantification can be used to obtain the mean total DAPI intensity per nucleus as well as the average volume occupation of one cell. These values are used to compute the number of nuclei (*num_nuc*) and the volume of the acinus in single cell volume unit (to allow direct comparison with the simulations). (C) Comparison of computer counts and manual count for the number of nuclei per acini.

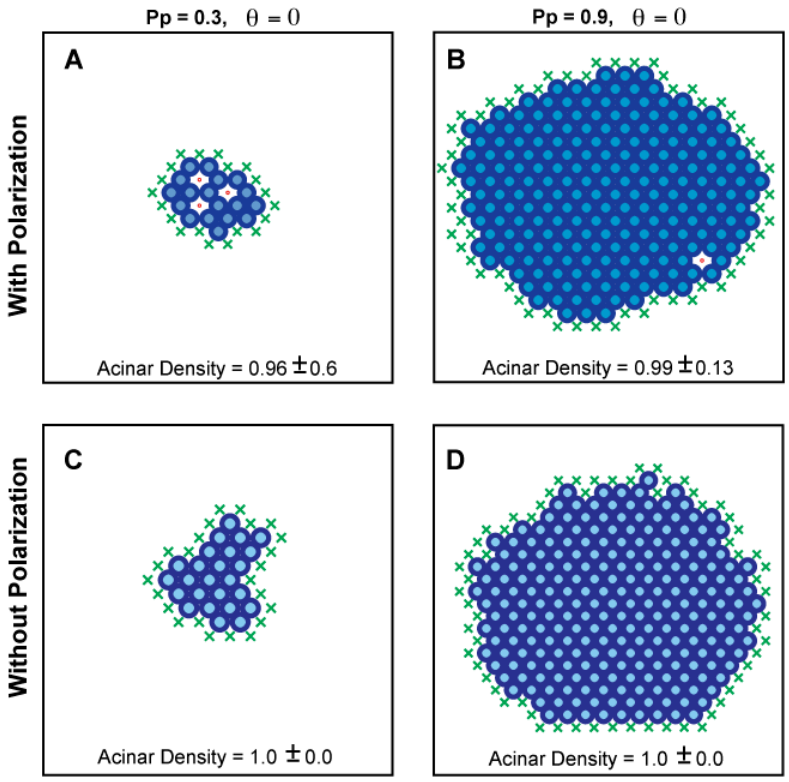

Fig. S2. Is polarization sufficient for lumen formation? (A-D) Snapshots of various simulations in the extreme case where apoptosis is turned off (θ=0) with either high/low proliferation and on/off polarization. (A) Polarization on, Pp=0.3. (B) Polarization on, Pp=0.9. (C) Polarization off, Pp=0.3. (D) Polarization off, Pp=0.9.

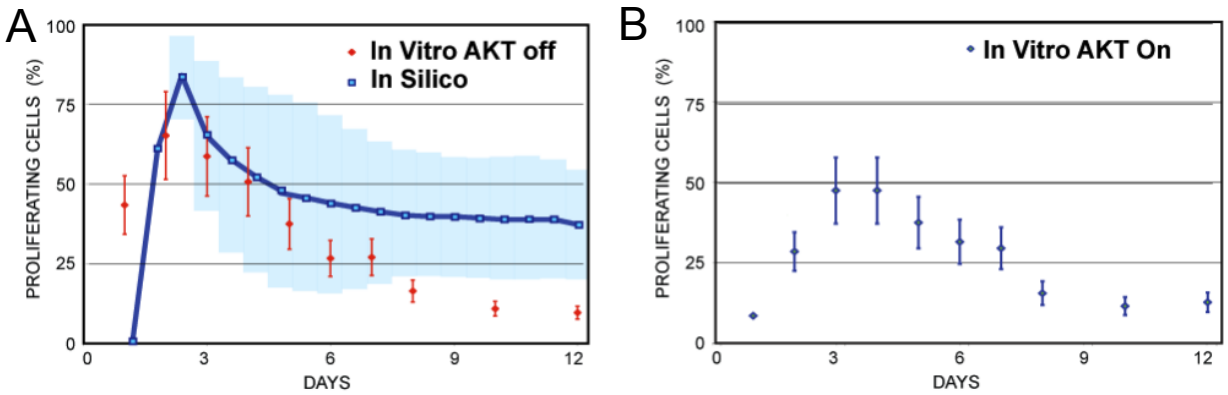

Fig. S3. Proliferation measurement. (A) Comparison of *in vitro* measurements of proliferation for normal MCF10A (Akt off - red diamonds), versus predicted levels of proliferation across time averaged over 100 *in silico* acini (solid blue line), using the normal phenotype conditions: θ=0.9, Pp=0.4. (B) *In vitro* measurements of proliferation for DCIS MCF10A model (Akt on - blue diamonds). No predictions are shown for these data.

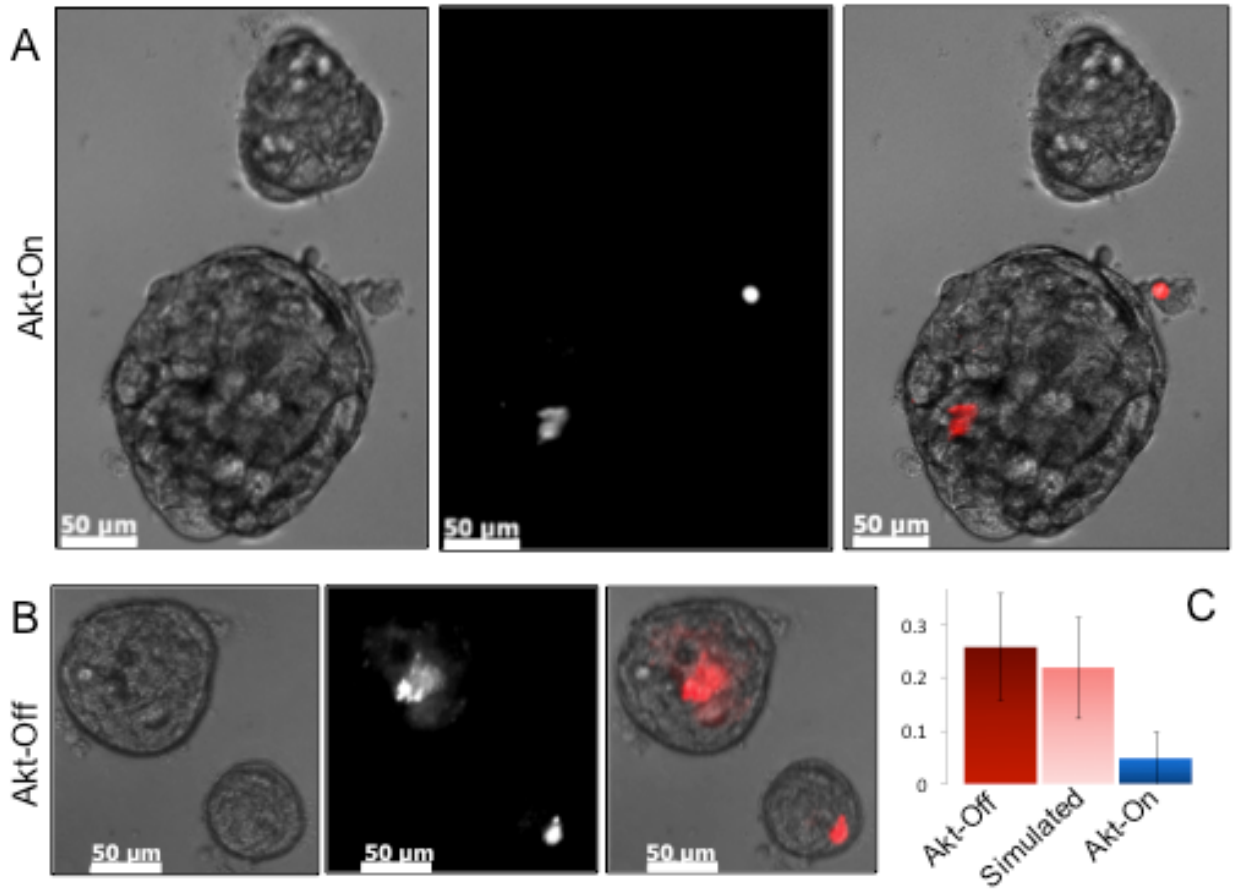

Fig. S4. Death measurement. (A-B) *In vitro* measurements of cell death at day 12 using Ethidium homodimer-1 (LIVE/DEAD kit, Invitrogen, Inc.), showing up in red channel (middle panel). Phase channel is shown on left panel and merged channel on the right. Red channel was acquired as a 3D stack with 5 µm step and positive cells were counted as previously described in Materials and Method for proliferation using ki67 labels. (A) 94 MCF10A acini with Akt-On were analyzed. (B) 116 MCF10A acini with Akt-Off were analyzed. (C) Average percent cell death for both *in vitro* systems and for simulated acini with the normal phenotype using conditions: θ=0.9, Pp=0.4

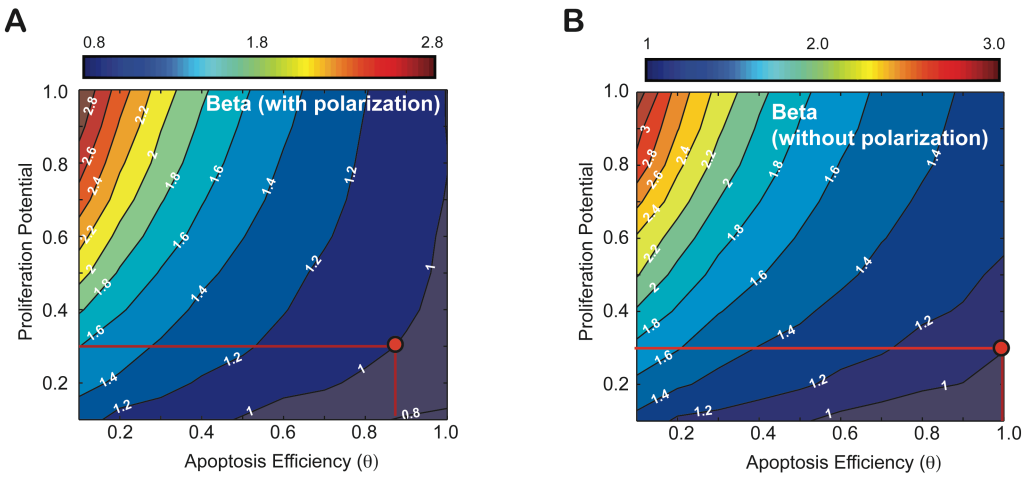

Fig. S5 Comparing the average number of epithelial layers (β) between polarization on and off. (A) β transition map when polarization is on. (B) β transition map when polarization is off. One can determine the level of apoptosis necessary to induce a normal epithelium (β=1) at a given level of proliferation (e.g. Pp=0.3). This is shown as a vertical red line intersecting the 1.0 isocontour on both maps (A and B). It is interesting to note that for equal proliferation, apoptosis levels must be significantly higher to induce a normal epithelium without polarization.

Movie S1 Example in silico simulation of mammary acinus formation. Parameters used were θ=0.9, Pp=0.4 and polarization was enabled. A snapshot of a cross-section is shown at the end of the movie.

Movie S2 Example in silico simulation of mammary acinus formation. Parameters used were θ=0.9, Pp=0.4 and polarization was disabled. A snapshot of a cross-section is shown at the end of the movie.