

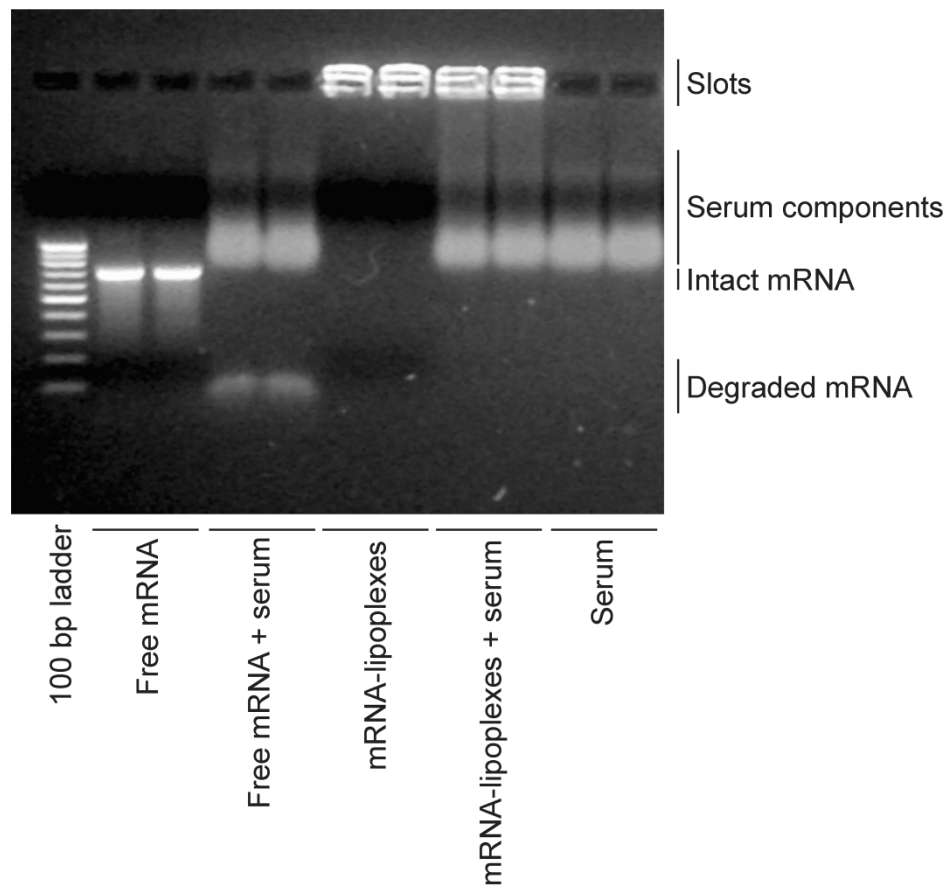
### SUPPLEMENTARY INFORMATION

**Supplementary Video 1: CEUS imaging of a vast lymphatic network in an intact female dog.** After s.c. injection of unloaded microbubbles around the mammary glands of an intact female dog, a vast lymphatic network could be observed with CEUS imaging.

**Supplementary Video 2: CEUS imaging of 2 lymph vessels connected to one lymph node.** Images were recorded after s.c. injection of mRNA-loaded microbubbles in an intact female dog.

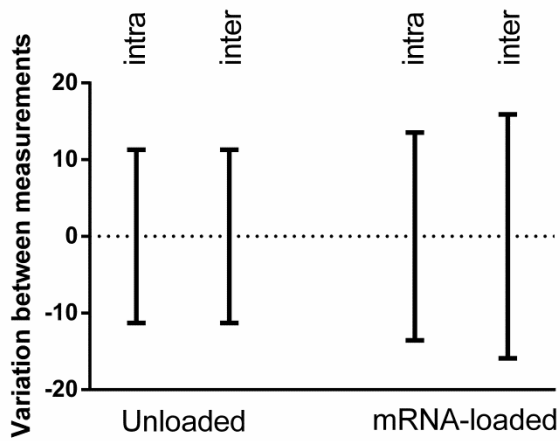
**Supplementary Video 3: CEUS of mRNA-loaded microbubbles 6 min after mRNA-loaded microbubble injection.** Images were recorded 6 min after injection of mRNA-loaded microbubbles in a spayed female dog.

**Supplementary Video 4: Burst destruction of intranodal microbubbles.** After injection of unloaded microbubbles in an intact female dog, multiple bursts were delivered to destroy the intranodal microbubbles and reduce the mean echo intensity.



**Figure S1: mRNA packaged in mRNA-lipoplexes is protected against degradation.** Gel electrophoresis was performed on free (unpackaged) mRNA and mRNA-lipoplexes. When free mRNA was incubated for 30 min with bovine serum, all the mRNA was degraded. In contrast, when the mRNA was formulated in mRNA-lipoplexes, serum addition did not lead to mRNA release, and no signs of degraded mRNA could be observed. As serum contains various components that also show on gel electrophoresis, free serum (without any mRNA addition) was run as a control.

### Observer differences for migration distance



**Figure S2: Intra- and inter-observer variability for migration distance measurements.**

Presented intervals contain 95% of the differences between two measurements of the same observer (intra) or measurements made by two independent observers (inter) of the migration distance of unloaded and mRNA-loaded microbubbles.