

Purpose: Growing concern with rising costs of preclinical testing of anti-tumor drugs in animal models creates demand for improvements in measurement accuracy. Caliper tumor volume measurements are the most commonly accepted parameter in tumor response studies. High frequency ultrasound (~35 MHz) is more accurate and the least expensive imaging measurement device for rodent tumors. The accuracy of US measurements is unfortunately highly dependent on operator performance and training. Although commercial phantoms for quality assurance (QA) in clinical ultrasound are common no source of QA phantoms was available to validate the accuracy of tumor response to chemotherapeutic agents in rodent models. **Method and Materials:** For these studies a special purpose ultrasound (US) phantom was designed using Gammex ultrasound materials and manufacturing expertise from clinical radiology. The prototype phantom is composed of four parts; A) high contrast uniformly spaced wire tool to measure vertical (depth) accuracy, horizontal accuracy and linearity, B) low contrast variable diameter cylinder accuracy tool at uniform depth, C) low contrast cylinder 2mm-diameter accuracy at variable depth tool and D) low contrast hyperechoic spheres to measure tumor volume accuracy. US images of the phantom were acquired and tumor volume measurements made with a 35MHz ultrasound Vevo 707 Visualsonics Rodent Imager. **Results:** The measurements showed that the errors are generally less than $\pm 5\%$. Large inter-operator errors approaching 50%, however, were observed due to 1. insufficient training, 2. undeveloped measurement protocols and 3. simple operator errors. **Conclusions:** The materials and manufacturing procedures for Gammex US phantoms for human studies can be used with smaller imaging objects suitable for mouse models. Preliminary experience shows potential for improved inter-institutional variability by improving measurement protocols and operator training. These phantoms are expected to improve small animal tumor response measurements, and reduce the cost of cancer drug testing by improving confidence levels of outcomes.