Preemergence herbicides (PREs) are a critical component of weed management in cotton, especially with the prevalence of glyphosate-resistant *Palmer amaranth*. The challenge in using PREs is the potential injury to seedling cotton. Previous research has indicated that a larger seed size can compensate for certain early season stresses. Field trials were replicated at three locations in 2021: The PDREC in Florence, SC, the EREC in Blackville, SC, and the Upper Coastal Plain Research Station in Rocky Mount, NC. Two seed sizes, a large and a small, were planted in early May at each location. Following planting, Reflex, Direx, and Warrant were applied to plots alone and in combination at high rates with a non-treated check included for each seed size. Data collection consisted of visual injury ratings at various days after planting (DAP), biomass weights at 3-leaf stage, plant heights, stand counts, yield, lint percent and fiber quality. Results from 2021 show that the large-seeded variety had a higher dry weight at the 3 leaf stage which could suggest it was less impacted by the PRE herbicide injury. This may mean that a larger, more vigorous seed could offer some protection when using PREs in cotton. However, at 42 DAP, both varieties appeared to “grow out” of the herbicide injury and the larger seed did not contribute to higher lint yield than the smaller seed. This study will be repeated in 2022 and results will hopefully be useful to cotton growers regarding seed size and PRE herbicide recommendations.