Orthostatic intolerance after space flight is still an issue for astronaut health. No in-flight countermeasure has been 100% effective to date. NASA currently uses an inflatable anti-gravity suit (AGS) during reentry, but this device is uncomfortable and loses effectiveness upon egress from the Shuttle. The Russian Space Agency currently uses a mechanical counter-pressure garment (Kentavr) that is difficult to adjust alone, and prolonged use may result in painful swelling at points where the garment is not continuous (feet, knees, and groin). To improve comfort, reduce upmass and stowage requirements, and control fabrication and maintenance costs, we have been evaluating a variety of gradient compression, mechanical counter-pressure garments, constructed from spandex and nylon, as a possible replacement for the current AGS. We have examined comfort and cardiovascular responses to knee-high garments in normovolemic subjects; thigh-high garments in hypovolemic subjects and in astronauts after space flight; and 1-piece, breast-high garments in hypovolemic subjects. These gradient compression garments provide 55 mmHg of compression over the ankle, decreasing linearly to ~35 mmHg at the knee. In thigh-high versions the compression continues to decrease to ~20 mmHg at the top of the leg, and for breast-high versions, to ~15 mmHg over the abdomen. Measures of efficacy include increased tilt survival time, elevated blood pressure and stroke volume, and lower heart-rate response to orthostatic stress. Results from these studies indicate that the greater the magnitude of compression and the greater the area of coverage, the more effective the compression garment becomes. Therefore, we are currently testing a 3-piece breast-high compression garment on astronauts after short-duration flight. We chose a 3-piece garment consisting of thigh-high stockings and shorts, because it is easy to don and comfortable to wear, and should provide the same level of protection as the 1-piece breast-high garments evaluated in hypovolemic test subjects.