Impact of body composition on pharmacokinetics of doxorubicin in pediatric patients: A Glaser Pediatric Research Network study. *S. L. Berg, L. Bomgaars, C. Twist, K. Matthay, T. Moore, D. Wypij; Texas Children's Cancer Ctr, Houston, TX; Stanford Univ Sch of Medicine, Palo Alto, CA; Univ of CA at San Francisco, San Francisco, CA; Univ of CA at Los Angeles, Los Angeles, CA; Harvard Medcl Sch, Boston, MA*

Background Body composition affects various physiologic processes involved in the distribution, metabolism, and elimination of drugs. Therefore body composition might be related to important pharmacokinetic (PK) parameters like clearance or half-life. These relationships have never been systematically studied for doxorubicin (dox) and its metabolite doxorubicinol (doxol). In addition, the PK behavior of dox and doxol have not been thoroughly described in children. In this study we evaluated the relationship between body composition and doxorubicin PK in children. **Methods** Eligible subjects were ≥ 1 and ≤ 21 years old; weighed ≥ 12 kg; received dox administered as an infusion of any duration < 24 hours, on either a 1-day or 2-day schedule; had ALT/AST ≤ 3 times the upper limit of normal and bilirubin $\leq$ upper limit of normal tested within 14 days prior to dox; and provided informed consent/assent. Blood samples were drawn prior to dox administration, at the midpoint of the infusion and at 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, and 48 hours after the infusion for 1-day schedules, or at 0, 0.5, 1, 2, 4, and 6, hours after the day 1 infusion and immediately prior to the day 2 infusion, then at 0, 0.5, 1, 1.5, 2, 4, 6, 8, 12, 24, and 48 hours after the day 2 infusion for 2-day schedules. Body composition was determined using dual-energy x-ray absorptiometry (DXA). Body mass index (BMI) was calculated from height and weight. Dox and doxol concentrations were analyzed by reverse-phase high-pressure liquid chromatography with fluorescence detection. Dox plasma PK were analyzed with maximum likelihood estimation as implemented in ADAPT II. **Results** Data are available for 16 subjects (12 male; 8 Hispanic, 6 Caucasian, 2 Asian). The median age is 15 years (range 3–21). The median % body fat by DXA is 22 % (range 16–36). The median BMI is 20 (range 14–30). The median dox clearance is 382 ml/m^2/min (range 141–768). The median terminal half-life is 30.6 hr (range 18.1–146.6). Dox clearance decreases with increasing BMI ($r=-0.56$, $P=0.02$) and tends to decrease with increasing % body fat ($r=-0.43$, $P=0.10$). **Conclusions** Potential relationships between increasing BMI, decreasing dox clearance, and dox toxicity should be explored.