**Background and Methods**

**Background:** *Staphylococcus epidermidis* is a ubiquitous human commensal but also a leading cause of healthcare-associated bloodstream infections (HABSI). Commensal *S. epidermidis* strains are genetically diverse. We used whole genome sequencing (WGS) to test the hypothesis that invasive *S. epidermidis* strains are genetically heterogeneous.

**Methods:** *S. epidermidis* isolates that caused a clinically significant HABSI from unique patients at the MD Anderson Cancer Center were collected between 2013 and 2015. WGS was performed via Illumina Miseq followed by phylogenomics using kSNP. Clinical metadata was abstracted from the EMR. A cluster was defined as ≥ 3 strains that differed from each other by ≤ 40 single nucleotide polymorphisms (SNPs) over the ~2.5 million base pair genome.

**Results**

Figure 2. Whole genome based identification of clusters of invasive *S. epidermidis*. Maximum-likelihood (ML) tree was reconstructed on an alignment of 56,124 core SNPs.

Figure 3. Identification of highly clonal strains of *S. epidermidis*. Data shown are number of SNPs separating individual strains stratified by ST. 50 strains had ≤ 10 SNPs relative to their nearest relative consistent with being nearly genetically identical.

Figure 4. Identification of underlying cancer-*S. epidermidis* cluster associations. *P* value refers to χ² test.

Figure 5. ST5B strains were isolated significantly later in the study period consistent with introduction followed by outbreak. *P* value refers to Kruskal-Wallis test.

**Conclusions**

- Majority of *S. epidermidis* invasive infections were caused by a limited number of highly clonal strains.
- These clones are not the predominant commensal forms of *S. epidermidis* found in healthy humans.
- It is likely that invasive clones of *S. epidermidis* are circulating in the hospital environment and may be susceptible to infection control initiatives.