Can whole genome sequencing assist in the detection of leiomyosarcoma?


Introduction
• Leiomyosarcoma is a uterine malignant tumour of smooth muscle / mesenchymal origin
• Most sarcomas arise independent of benign leiomyomas
• No pre-op investigations have been shown to be useful

Objective
• To investigate whether plasma DNA sequencing using a clinical whole genome – non-invasive prenatal testing (NIPT) platform can distinguish leiomyosarcoma from benign leiomyomas

Hypothesis
• Pre-symptomatic maternal malignancies have been incidentally detected during NIPT based on abnormal genomic profiles.
• Low coverage sequencing approach could have potential to distinguish between leiomyosarcoma and a benign fibroid to give a laparoscopic surgeon confidence to morcellate in the non-pregnant population.

Methods
• Case control of 24 plasma samples (Jan 13 to Aug 15)
• 4 recurrent metastatic LMS (plasma and tissue samples) collected. Benign controls confirmed histologically leiomyomas.
• Sequencing data blindly analyzed
  1. Subchromosomal changes using an open source algorithm (WISECONDOR). Genomic gains or losses ≥ 20 Mb prespecified as “screen positive” calls. Mapped to recurrent copy number variations reported in cancer genome atlas.
  2. Selected whole chromosome gains or losses reported using NIPT.

Results
• Detected 1/4 cancer cases using the subchromosomal analysis (specificity 86% (95% CI 0.66 -0.97)).
• 20 benign controls did not have any subchromosomal gains ≥ 20 Mb. NIPT - 1 “monosomy 18” call from cancer group.
• No false positive results.

Conclusion
• Low coverage plasma DNA sequencing and chromosomal analysis for chromosomal CNVs>20 Mb used for prenatal testing detected 1 in 4 of all Leiomyosarcoma, with all 20 out of 20 benign controls screening negative.
• Our findings demonstrate the potential of a high throughput sequencing platform to use as pre-operative test for LMS.