
A Part of the Q-CROC-01 Project

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No conflict of interest to declare
Personalized Medicine – the present and future of medicine!

• It’s at our door!
• Part of person-centred care
• Goal: find “the right treatment for the right patient”
• In oncology:
  • developing personalized tailored therapies, based on genetic and molecular diagnostic tests
  • minimize cancer resistance, improve efficacy of cancer therapy
  • E.g.: Breast cancer specific targeted therapies, based on Her-2/Neu gene amplification (trastuzumab), ER, PR (adjuvant tx tamoxifen, aromatase inhib)
• Multidisciplinary approach, from bench to bedside
  ➔ a.k.a. “Translational Research”
From cancer genomics to personalized medicine

https://kcryan.wordpress.com/2010/08/26/donna-dickenson-on-personalised-medicine/
Q-CROC – a Multicentric Translational Study

• “Quebec Clinical Research Organization in Cancer”
• Patient stratification to different chemotherapeutic regimens based on their molecular genetic profile
  • Serial tumor biopsy before and after chemotherapy for genomics analysis
  • Who is resistant and why? Personalized response?
  • Tailoring chemotherapy for each person
• Radiology key role: serial tumor biopsies for genomics analysis, post-treatment imaging
• Different cancers studied (breast, NHL, colon)
• Q-CROC-01: colorectal cancer liver metastases
Rationale

• Liver biopsies for **genomics profiling**, not just histopathology!
• **Current Technique:** Standard Operating Procedure (SOP) for ultrasound-guided targeted liver biopsies, based on ACR recommendations
• **Challenge:** criteria for biospecimen adequacy are different for standard histopathology vs genomics analysis
  • Genomics analysis requires higher content of nucleic acids/tumor cells

**Question:** Is the current SOP going to yield a sample adequacy rate for genomics similar to or worse than that for histopathology analysis?
  • **adequacy rate in the literature = 70-90%** [5]

• First influential variable = tissue sampling by IR!
Objectives

• Determine adequacy rate of biospecimens for molecular profiling, using the current standard operating procedure for targeted liver biopsy
• Determine factors that influence biospecimen adequacy
• Compare our adequacy rate with that of the literature and that proposed by the ACR (75%)

Optimize biospecimen quality for molecular & genomics profiling
Materials and Methods

**Inclusion Criteria:**
- confirmed CRC with at least one liver metastasis
- confirmed liver metastasis
- patient not initially resectable
- scheduled for first line chemox
- adequate coag profile
- life expectancy $\geq 12$ weeks

**Exclusion Criteria:**
- resectable liver met
- prior therapy for metastatic cancer
- non-diagnostic specimen path
- contraindication to chemox
- brain mets
- pregnant or breastfeeding
- HIV +ve
Materials and Methods

- Baseline CT scan and liver metastasis biopsy (by US) pre-chemotx
- Chemotherapy
- Response evaluation at 8 weeks, then q12weeks with CT
- Re-biopsy liver metastasis if there is recurrence
Liver Biopsy Technique

• 3 needle passes (3 core biopsy samples)
• Evaluation of tissue sample contents: %tumor material (>=50% required), tumour cellularity (>=60% required), necrosis, and stroma

Three liver biopsy passes

1. PBS WASH
2. RNA later
3. Formalin

Frozen biopsy
- Confirm histology (determine % tumor)
- Delineate tumor cells
- Cut
- DNA/RNA Isolation

Harvest Vectastain

FFPE (s)
Liver Biopsy – Standard Operating Procedure

- US-guided by IR
- Conscious sedation
- Sterile draping, local anesthetic
- Free-hand technique
- BioPince™ end-cutting core biopsy device (16- or 18-gauge), Tru-Cut core biopsy device (18-g), or Temno device (18-g)
- Samples put in respective vials, kept at 4°C and shipped immediately to Central Pathology Lab
- Patients kept for observation x 4-6 hours
Statistical Analyses

• Outcome variables:
  • biospecimen adequacy for genomics analysis
  • % tumour cellularity and % tumour content
• Comparison btwn 1\textsuperscript{st} and 2\textsuperscript{nd} tissue samples: paired t-test and Chi-square test
• Comparison btwn types of needles (TruCut, Biopince, Temno): One-way ANOVA and Chi-square test
Results—Subject flowchart

- 72 enrolled
  - 63 included (125 samples)
    - 62 with 2 biopsy samples (124 samples)
    - 1 with 1 biopsy sample (1 sample)
  - 9 excluded
    - No prechemotx biopsy, negative biopsy, withdrawn consent

Nb of samples for genomics analysis
Results

• Among 62 patients, overall biospecimen adequacy rate 85.5%

• Among 125 biospecimens, adequacy rate was 65%
Results

• Biospecimen adequacy for genomics analysis:
  • No significant difference between 1st and 2nd tissue samples (p=0.852)
  • No significant difference between needle types (p=0.239)

• % Tumor material and % Tumor cellularity:
  • No significant difference between 1st and 2nd tissue samples (p=0.542; p=0.065)
  • No significant difference between needle types (p=0.252; p=0.393)
Discussion

• Biospecimen adequacy rate for standard pathology:
  • In the literature: 70 to 90%
  • Recommended by the ACR: >=75%

• Our adequacy rate for genomics analysis:
  • Per patient: 85.5%
  • Per needle pass: 65%

• Good results compared to recommendations

• Results confirm need for at least 2 needle passes to reach recommended adequacy rate
Conclusion

- Standard Operating Procedure for US-guided targeted liver biopsy is satisfactory in tissue sampling for genomics analysis
  - Good adequacy rate compared to literature and recommendations
- The order of sampling ($1^{st}$ versus $2^{nd}$ needle pass) and the type of biopsy needle does not influence the adequacy rate nor tumor cell content.
- At least 2 needle passes are required per patient to obtain a satisfactory adequacy rate.
Future Directions

• More patients are being recruited; final analyses will ensue
• Comparison with the 3rd tissue sample in progress
• Comparison of location of targeted metastatic liver lesion
• Factor-in the experience of the operator
Thank you