1750TiP: Nanopore Sequencing for Fast and Accurate Breast Cancer Diagnosis in a resource-constraint setting: FAST-ABCD study

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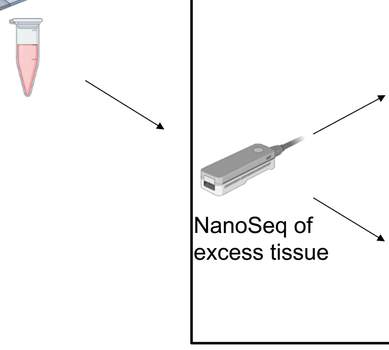
Background

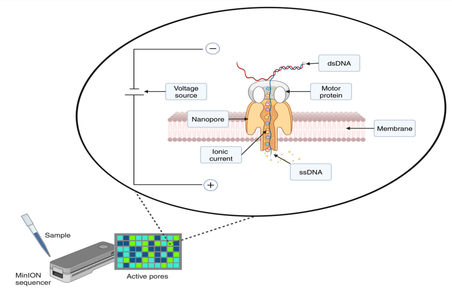
- Breast cancer (BC) is the most common cancer in women in Sub-Saharan Africa (SSA) and its incidence is projected to double by 2040[1].
- Optimal treatment depends on determining **ER, PR, and HER2** status.
- Only ~50% of pathology laboratories in SSA can perform **immunohistochemistry (IHC) on site**[2].
- **Less than 10%** on BC cases in Tanzania are tested for ER, PR and HER2 status[3].
- **Delays of several weeks** between biopsy and diagnosis are common due to cost, limited infrastructure, and long IHC turnaround times[4].
- Accuracy of tumor diagnosis using nanopore sequencing has been validated, but existing data is mostly derived from retrospective studies
- **Kilimanjaro Christian Medical Center (KCMC)** is a zonal referral hospital, serves a population of 15 million people and has a 700-bed capacity



Diagnostic tool and Methods

Nanopore sequencing[5] (NanoSeq) offers a novel, rapid, cost-effective alternative:

- Provides genome-wide DNA methylation profiles and copy number alterations **within hours**.
- Enables determination of breast cancer subtype:
  - **HER2 copy number** for HER2+ status.
  - **Methylation profiles** as a proxy to distinguish luminal/HR+ from basal/triple-negative tumors.



- **Tissue processing & DNA extraction:** Tumor tissue is homogenized and processed using Qiagen DNeasy spin columns; DNA is eluted, quantified and quality-controlled.
- **Library prep & sequencing:** DNA libraries prepared with ONT Rapid Barcoding Kit (V14) and sequenced on MinION (R10.4.1); flow cells are reused for cost efficiency.
- **On-site bioinformatics (nanoDx):** Raw data analyzed at KCMC using the nanoDx pipeline for basecalling, alignment, copy number profiling and DNA methylation-based classification.
- **Subtype classification:** Combines HER2 copy number and methylation-based clustering (luminal vs. basal) to assign subtype: HER2+, HR+/HER2−, or triple-negative.

Trial Design

- Single center, prospective, observational trial
- Consecutive patients with suspected BC and indication for biopsy/surgery after specialist consultation will be enrolled

Inclusion criteria:

- Aged ≥ 18 with a clinical suspected breast cancer after specialist consultation and indication for biopsy or surgery
- Ability of patient to understand character and individual consequences of the trial and written informed consent

Exclusion criteria:

- Patients who have already commenced therapy for breast cancer (except for treatment other than biomedicine, e.g. herbal medicines)

Study Objectives

Primary endpoints

- Non-inferiority of nanopore-based biomarker evaluation vs. standard of care
- Turnaround-time
- Feasibility

Secondary endpoints

- Patient-reported outcomes
- Timeline through healthcare sercives

References

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MR declares no conflicts of interest