Clinical NGS testing landscape: Illumina to remain dominant, with competitors addressing niche opportunities based on differentiated platform attributes

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Primary and secondary research confirms that NGS is poised to explode in clinical settings for a variety of applications

We conducted an extensive review of over 1,000 peer-reviewed publications from 2012 through 2015 coupled with 30 in-depth interviews with key opinion leaders to assess key trends in clinical NGS.

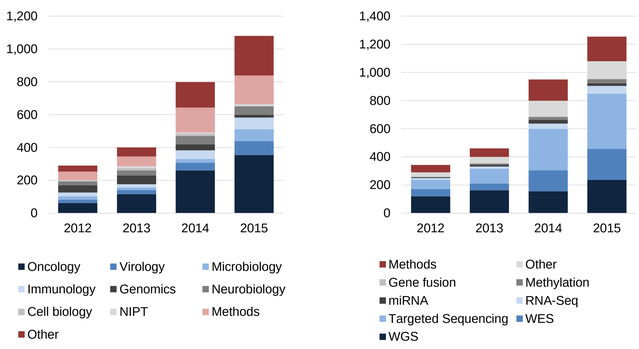
Our research indicates that clinical NGS is in a rapid growth phase driven primarily by adoption in oncology, rare diseases and NIPT. Within oncology, NGS use is correlated with tumors with high disease burden and availability of targeted therapies in which NGS could help optimize care (primarily breast, lung, CRC).

While clinical NGS adoption is exceeding even the most bullish forecasts, many institutions are unprepared to leverage the full potential of the technology, primarily due to workflow complexity, including in the front-end (i.e. sample preparation complexity compared to other fully automated methods) and the back-end (i.e. data analysis). A number of novel solutions may address these issues (e.g., Ion Torrent S5, Qiagen GeneReader) and compete with Illumina on dimensions other than throughput and data quality (e.g., turnaround time, sample to answer solutions).

Illumina is expected to remain dominant in the platform market for clinical NGS with sustained innovations expected across multiple platforms within their portfolio. However, nanopore sequencers are quickly improving their accuracy and may represent a disruptive threat (using the Christiansen framework for disruptive innovation). Their performance is expected to soon meet the needs of lower performance clinical applications with the upside potential to disrupt established technologies (e.g., SBS) given their scalability.

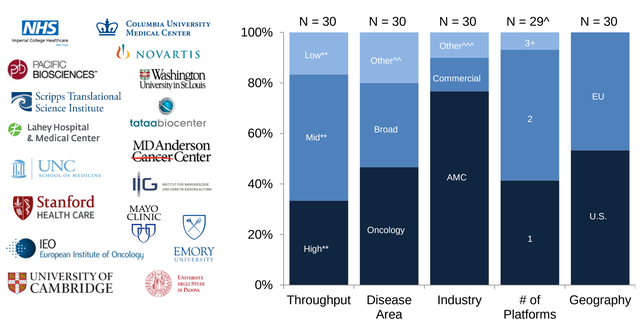
A publication analysis of 1,285 clinical papers indicates that NGS is being used beyond oncology and NIPT, and that targeted sequencing is gaining relative share

Analysis of Peer-Reviewed Clinical Publications



We interviewed 30 experts; while their feedback confirms Illumina's dominance, Ion Torrent appears to compete effectively for solid tumor testing

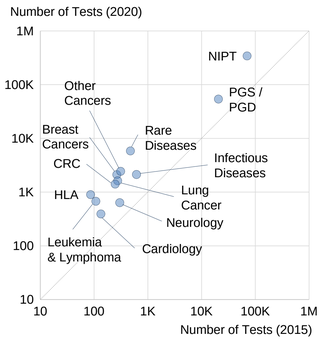
Interviewee Demographics (N=30)



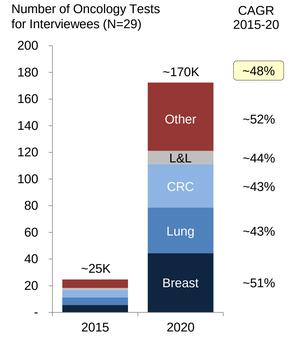
Note: * List not exhaustive; ** Low throughput ≤100 tests / year, mid throughput = 100 – 1000 tests / year, high throughput ≥1000 tests / year;
^ 1 interviewee provided qualitative feedback only; ^^ Includes non-invasive prenatal testing and infectious diseases; ^^^ Includes KOL's and other experts in NGS
Source: DeciBio Interviews and Analysis

Interviewee feedback indicates that clinical oncology NGS testing volumes may increase ~7x at some leading centers alone over the next 5 years

Average Yearly Volumes by NGS Test Types (2015-2020)



Number of Oncology Tests for Interviewees (N=29)

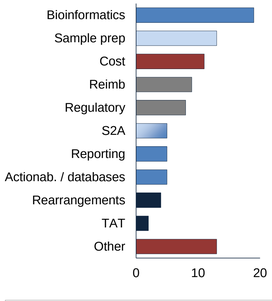


CAGR 2015-20

~48%
~52%
~44%
~43%
~43%
~51%

The majority of Interviewees agree that NGS unmet needs are now on the front- and back-end of the workflow

Clinical NGS Unmet Needs (N=30)



Key:
Sequencing | Pre-Seq. | Post-Seq.
Regulatory & Reimburs. | Other

- Key front-end issues include:
  - Improved automation / sample-to-answer (S2A) options
  - Improved sample preparation solutions
  - *"… I don't think a lot of people fully appreciate the challenges associated with working with degraded FFPE DNA, let alone small DNA amounts available from liquid biopsies …"*

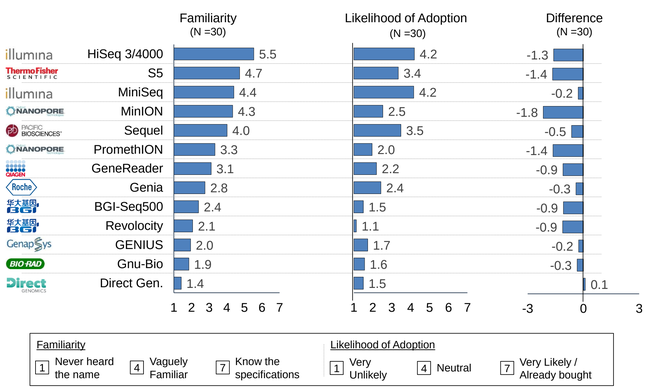
  Interviewee Feedback
- Key back-end issues include:
  - Improved reporting and analysis of variants of unknown significance (VUS)
  - Improved bioinformatics solutions (e.g., for variant prioritization)
  - *"… Right now, you get different answers if you put WES data through different pipelines – that's a big "no-no" for the FDA, as result consistency across institutions is critical …"*

  Interviewee Feedback

Note: * Other unmet needs include: improved tech support, improved whole genome public datasets, improved data interpretation tools, improved solutions for low DNA amounts, solutions for fast evolving cancer panels, help with technology incorporation into clinical practice, availability of kits with increased sensitivity and specificity, availability of more automation solutions, availability of longer reads, solutions with decreased assay failure rates, incorporation into guidelines

While Illumina is expected to remain dominant, a subset of interviewees expressed interest in multiple novel platforms

Familiarity and Likelihood of Adoption of Select NGS Platforms

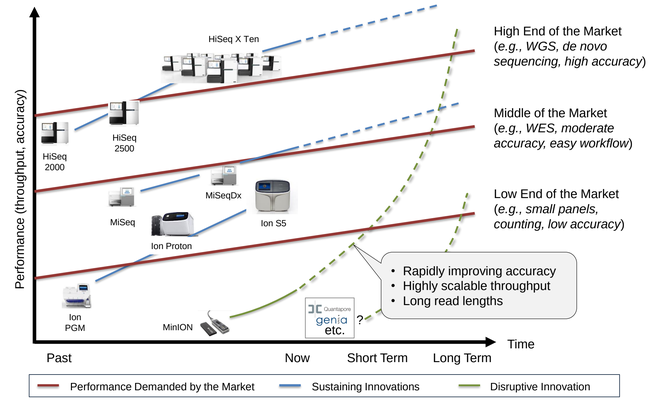


Familiarity
1 Never heard the name | 4 Vaguely Familiar | 7 Know the specifications

Likelihood of Adoption
1 Very Unlikely | 4 Neutral | 7 Very Likely / Already bought

Applying Christensen's disruptive innovation framework to NGS highlights that nanopore sequencing has characteristics of a potential disruptive innovations

Framework of Disruptive Innovation – NGS in Translational Research and Clinical Diagnostics



High End of the Market (*e.g., WGS, de novo sequencing, high accuracy*)

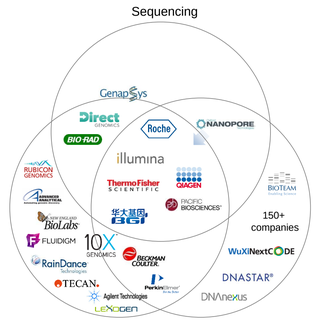
Middle of the Market (*e.g., WES, moderate accuracy, easy workflow*)

Low End of the Market (*e.g., small panels, counting, low accuracy*)

Source: "Innovators Dilemma" by Clayton Christensen; Company websites, DeciBio experience and analysis

NGS is an attractive space with opportunities for various companies to participate in this fast growing market

Select Players by Workflow Steps



- The number of companies offering sequencing technologies remains relatively limited
- Independent companies offering sample prep, automation, or bioinformatics solutions can address (sometimes niche) market needs
  - Tecan and Perkin Elmer have leveraged their automation expertise to offer sample prep solutions
  - Fluidigm and RainDance have applied their respective patent-protected technologies to NGS sample prep
  - Multiple smaller players offer library preparation solutions, differentiating their offerings on multiple dimensions
- While >150 companies offer DNA software packages, the lack of bioinformatics infrastructure and analytical tools continues to gate adoption for some customers
  - Large established research tools players have purchased large (e.g., Qiagen | Ingenuity) and small (e.g., Roche | Bina) bioinformatics companies

Note: * TAT: Turnaround Time
Source: Company Websites, DeciBio Analysis

While Illumina is expected to remain dominant in the short term, the clinical market may remain dynamic in the long term, with increased competitive intensity

Illumina is expected to remain dominant in the platform market for clinical NGS with sustained innovations expected across multiple platforms within their portfolio. However, nanopore sequencers are quickly improving their accuracy and may represent a disruptive threat (using the Christiansen framework for disruptive innovation).

Acknowledgements, authorship & disclaimer

We thank the panel of DeciBio experts that participated in this study

* These authors contributed equally to this work; † Poster presenter

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