



Circulating Nucleosomes for Detection of Colorectal Cancer and High-risk Advanced Adenomas

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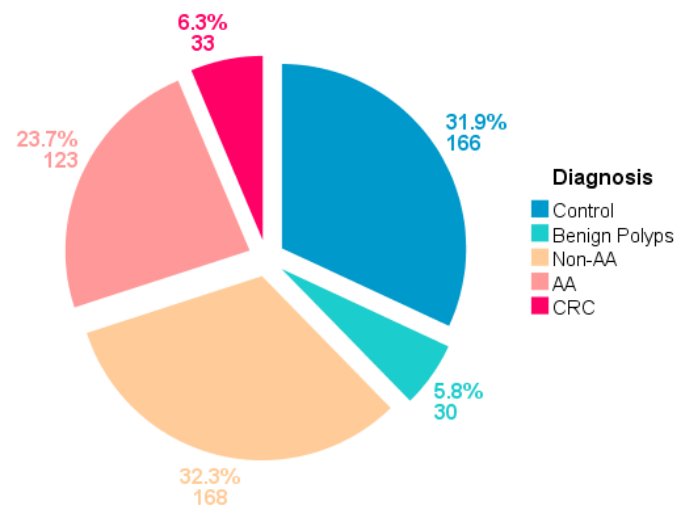
Background and aim

- Approximately **60%** of Fecal immunochemical tests (FITs) are **false-positive** and result in a lot of unnecessary colonoscopies.
- There is an unmet need for a simple test to supplement FIT to triage individuals at higher risk who require colonoscopy referrals.
- FIT is less effective in detecting **proximal** lesions even advanced neoplasms.
- We investigated the levels of circulating free nucleosomes containing different epigenetic modifications in patients referred for colonoscopy and the detection rate of proximal neoplasms.



Material and Methods

- 520 average-risk asymptomatic patients: (i) CRC (n= 33), (ii) advanced adenoma (AA) (n=123, including 18 with AA>2cm); (iii) non-AA (n=168); (iv) non-neoplastic polyps (n=30); (vi) colonoscopy negative control (n=166).
- Plasma and stool samples were obtained prior to colonoscopy.
- Circulating Nucleosome levels:
 - ✓ Nu.Q® quantitative immuno-assays: Belgian Volition SRL, Belgium.
 - ✓ 7 different assays measuring: H3.1-, H3K27Me3-, H3K36Me3-, H3K9Me3-, H3K14Ac-, H3K27Ac- and H3R8Cit-nucleosomes.
- FIT: OC-SENSOR (Eiken Chemical Co., Ltd., Tokyo, Japan) using positive cut-off of 20ug/g feces.



Results

Nu.Q[®] biomarkers (H3K27Me3 and H3R8Cit) plus FIT improved sensitivity for CRC and AA

Combination of two Nu.Q[®] biomarkers H3K27Me3 and H3R8Cit with FIT allowed:

- The detection of all CRC and 94.3% of AA, including all the high-risk adenomas.
- The detection of 50/55 proximal adenomas including 3 proximal AA >2cm not detected by FIT.

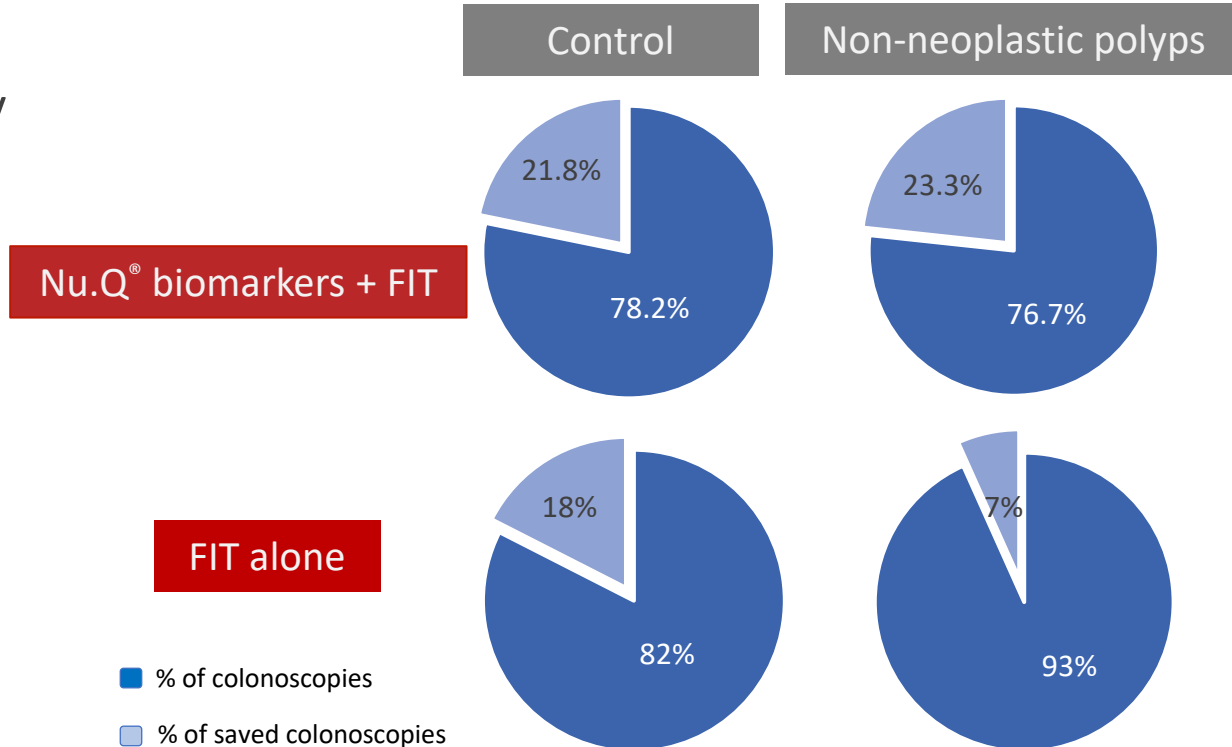


Diagnosis	Positive Triage Test	
	FIT	Nu.Q [®] + FIT
CRC	33/33	33/33
Advanced Adenoma (AA)	112/123	116/123
<= 1cm	45/48	43/48
1-2 cm	52/57	55/57
> 2 cm (high risk AA)	15/18	18/18
Non-AA	141/168	149/167
Non-neoplastic polyps	28/30	25/30
Control	137/166	131/165

Results

Nu.Q[®] biomarkers: H3K27Me3 and H3R8Cit plus FIT could reduce unnecessary colonoscopies

- The same combination could reduce unnecessary colonoscopies by 21.8% and 23.3% in control and non-neoplastic polyps subgroups respectively.



Conclusion

- H3K27Me3 and H3R8Cit-nucleosome levels in combination with FIT in a logistic regression model could:
 - ✓ Improve the detection of proximal high-risk AA
 - ✓ Provide a non-invasive method to reduce unnecessary colonoscopy
- Combination use of a nucleosome blood test with FIT may improve the effectiveness and could reduce the overall cost of FIT-based screening.