Introduction: Ki67; Average Versus Hot Spots; Eye Ball Versus Image Analysis

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Nothing to disclose

It is important to evaluate the status of cell proliferation in the tumor cells, with relation to clinical outcome, response to therapy and others especially in various endocrine tumors.

The value and pitfalls of Ki67 IHC in:
- Pancreatic neuroendocrine neoplasms
- Pituitary tumors
- Pulmonary neuroendocrine neoplasms
- Gastrointestinal neuroendocrine neoplasms
- Adrenal tumors

How to obtain clinically relevant cell proliferation data?

1. Counting the mitosis: easy but subjective.....
2. DNA contents: G1, S, M G2 phase flow cytometry, image cytometry: cumbersome
3. Uptake of BrdU, thymidine: accurate S phase indicator but clinically irrelevant
4. IHC of cell proliferation related nuclear antigen: PCNA: + in non-proliferative cells Topoisomerase I/II: the same as above Histone mRNA: mRNA ISH required
**Ki67: only detected in mid-G1, S, G2, M phase**


Initially only applicable in frozen tissue sections.

Now can be used in archival materials using MIB-1 mouse monoclonal antibody.

**Factors influencing the results of Ki67 labeling index**

Dowsett M et al., Assessment of Ki67 in breast cancer.

JCNI 2011; 103:1656-1664

Preanalytical (fixation or others)

must use 10% neutral buffered formalin as fixative

unstained slides to be used within 14 days if possible

Analytical (staining techniques)

Interpretation/scoring

Data handling (interpretation)

Nothing is more important than to standardize methods of preparation, staining and interpretation of Ki67 analysis in breast cancer patients.

**Recommendation in Ki67 LI in NET**

Identify the hot spots at low power

1. Use MIB1 antibody

2. Measure 500-1000 cells

3. Labeling index should be obtained.

Yes, results correlated with clinical outcome (G1,2 & 3)

However...

Fixation, Immunointensity

Numerous problems to be solved.

**Ki67 labeling index in PNET in 2017 WHO**

1. Capture “hot spots” through CCD camera following eye ball identification by a pathologist

2. Print the images

3. Count the percentage of Ki67 positive cells

**Automatic analysis difficulty in setting parameter**

- Overcount non-tumor cells
  (inflammatory cells, stromal cells etc.)

⇒ Extremely complicated pattern recognition for machinery parameters

⇒ Discrepancy from pathologist’s eyeballs in wide area

**Automatic analysis of Ki67 LI in 2017**

No standard platforms of evaluating Ki67 labeling index

No compatibility, Truth is ?????
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