Small lung biopsies in cytology – practical view

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Disclosure:

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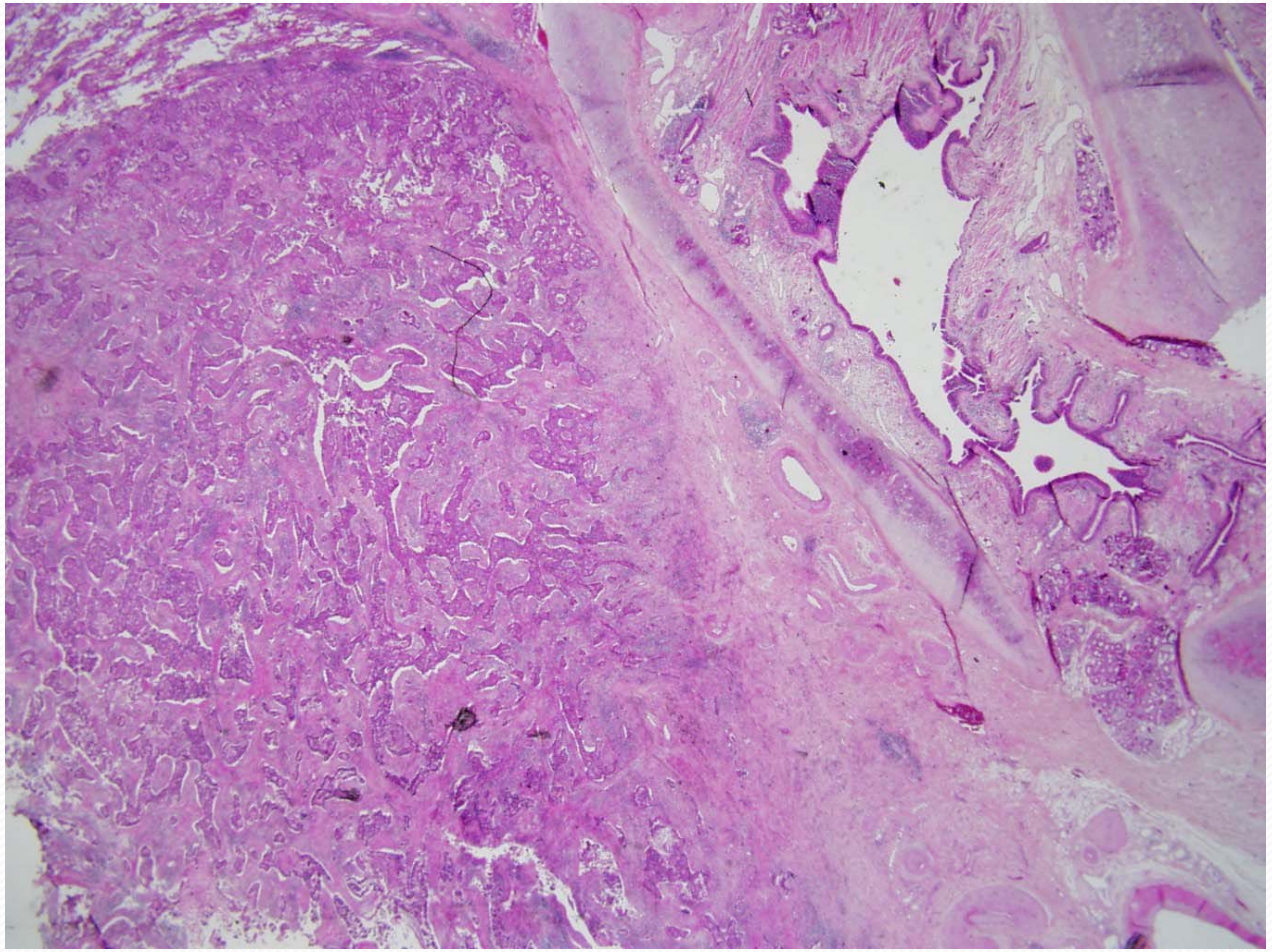
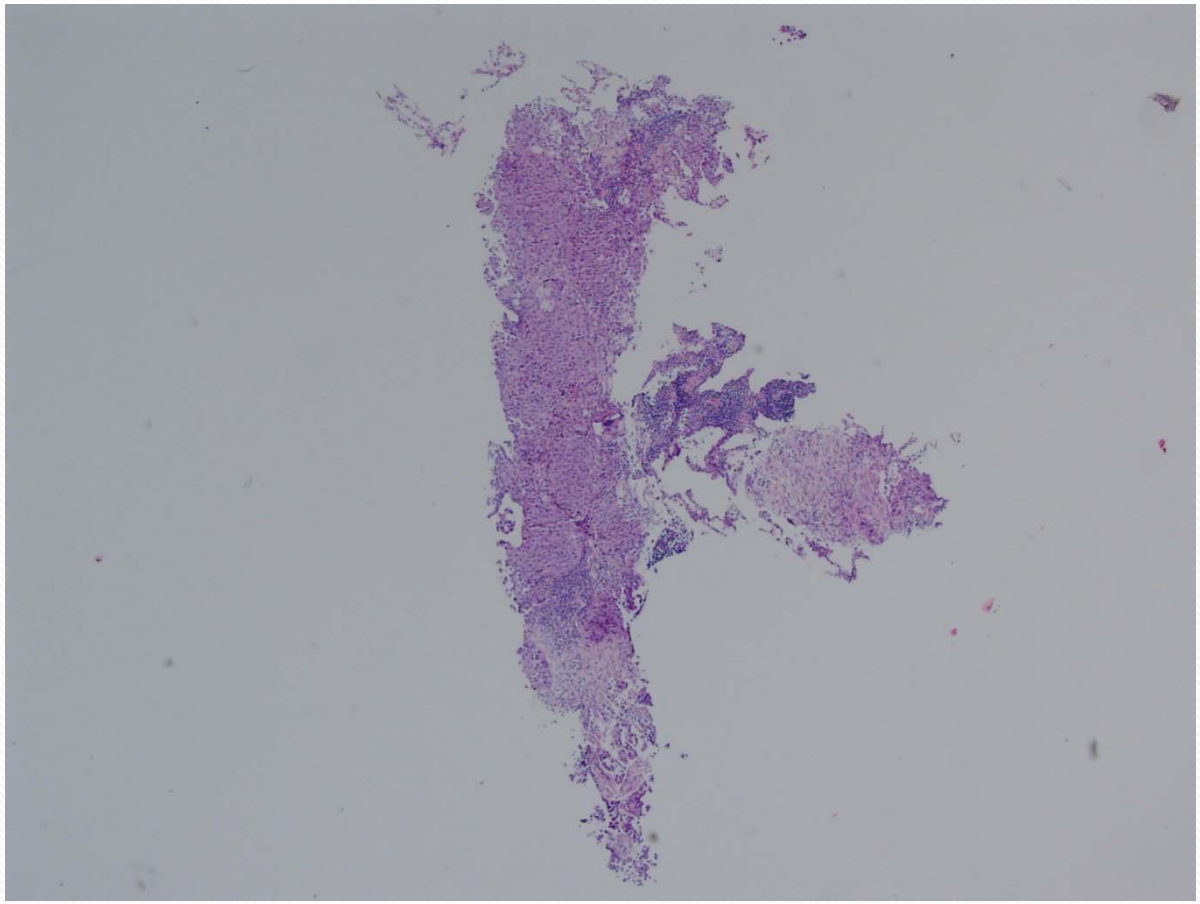
- I'm not a cytologist.
- This lecture is based on the efforts and experience the Hadassah Cytology Unit invested.

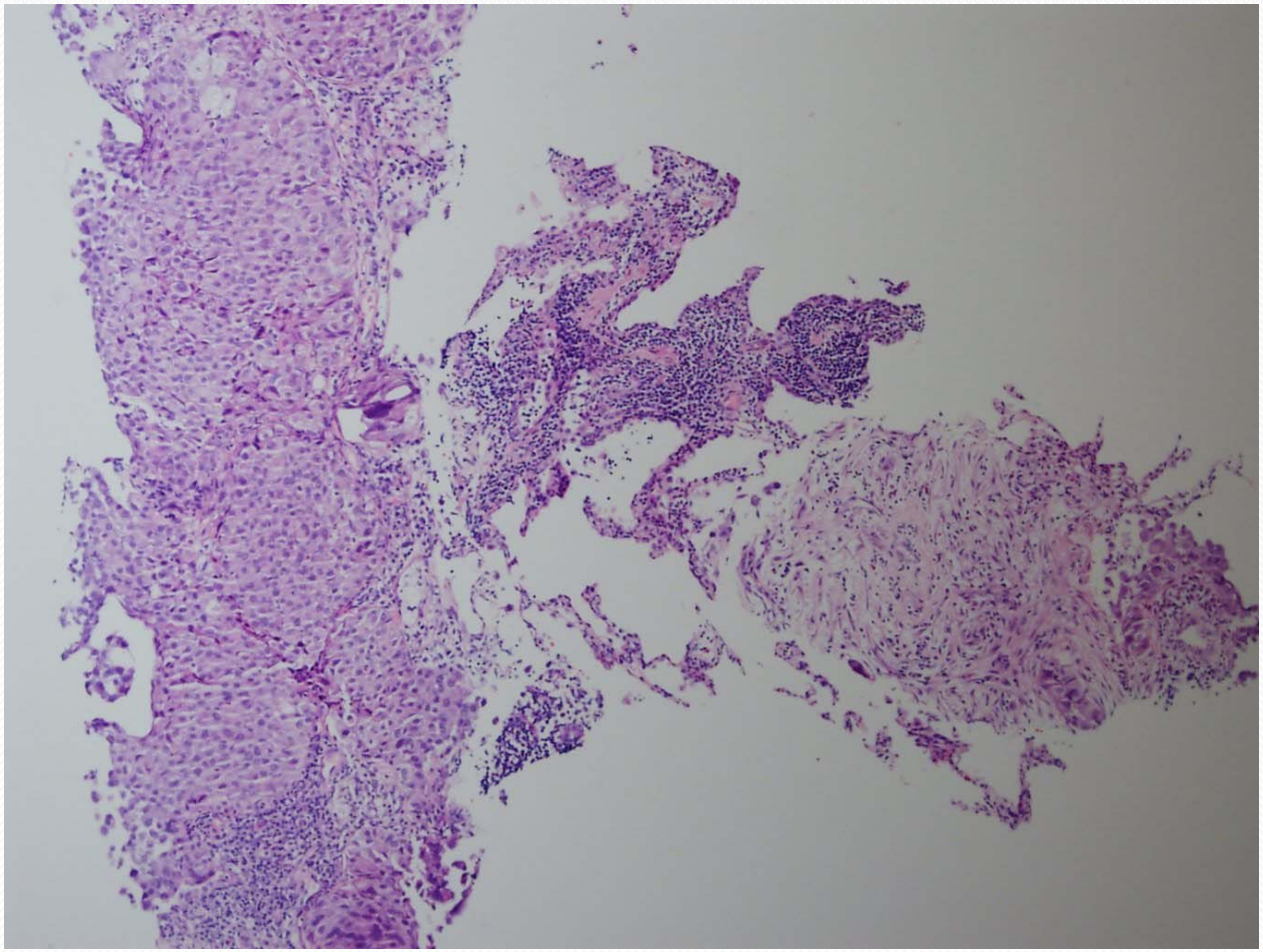
The optimum…



Real life… Optimum

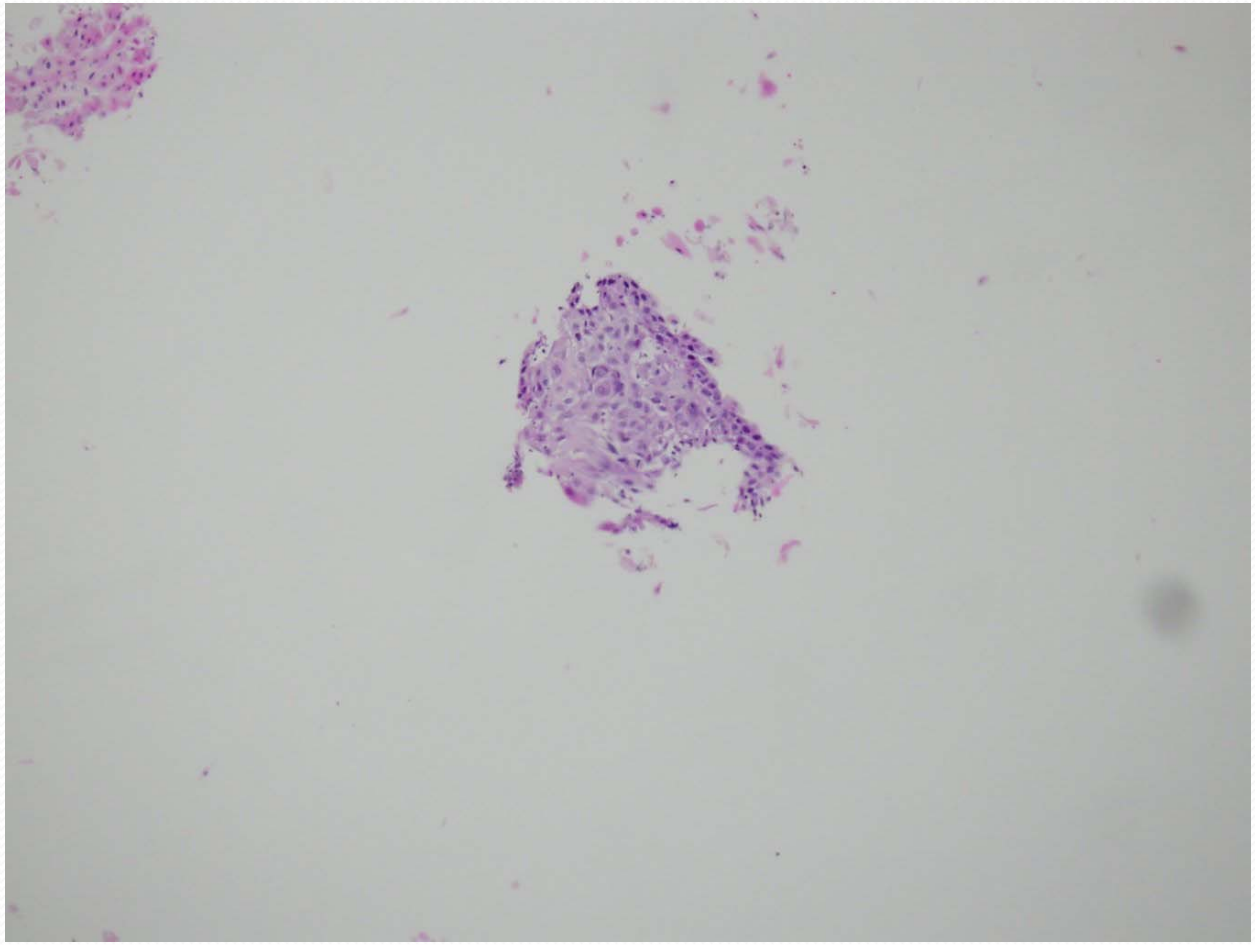


Real life…



Real life II

- Tissue is the Issue!



Lung Cancer 76 (2012) 1–18

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The challenge of NSCLC diagnosis and predictive analysis on small samples. Practical approach of a working group.

Thunnissen E[1], Kerr KM, Herth FJ, Lantuejoul S, Papotti M, Rintoul RC, Rossi G, Skov BG, Weynand B, Bubendorf L, Katrien G, Johansson L, López-Ríos F, Ninane V, Olszewski W, Popper H, Jaume S, Schnabel P, Thiberville L, Laenger F.

Author information

Abstract

Until recently, the division of pulmonary carcinomas into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) was adequate for therapy selection. Due to the emergence of new treatment options subtyping of NSCLC and predictive testing have become mandatory. A practical approach to the new requirements involving interaction between pulmonologist, oncologist and molecular pathology to optimize patient care is described. The diagnosis of lung cancer involves (i) the identification and complete classification of malignancy, (ii) immunohistochemistry is used to predict the likely NSCLC subtype (squamous cell vs. adenocarcinoma), as in small diagnostic samples specific subtyping is frequently on morphological grounds alone not feasible (NSCLC-NOS), (iii) molecular testing. To allow the extended diagnostic and predictive examination (i) tissue sampling should be maximized whenever feasible and deemed clinically safe, reducing the need for re-biopsy for additional studies and (ii) tissue handling, processing and sectioning should be optimized. Complex diagnostic algorithms are emerging, which will require close dialogue and understanding between pulmonologists and others who are closely involved in tissue acquisition, pathologists and oncologists who will ultimately, with the patient, make treatment decisions. Personalized medicine not only means the choice of treatment tailored to the individual patient, but also reflects the need to consider how investigative and diagnostic strategies must also be planned according to individual tumour characteristics.

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This is the main topic of the this talk

National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Non-Small Cell Lung Cancer

Version 4.2017 — January 18, 2017

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2017
Non-Small Cell Lung Cancer

NCCN Guidelines Index
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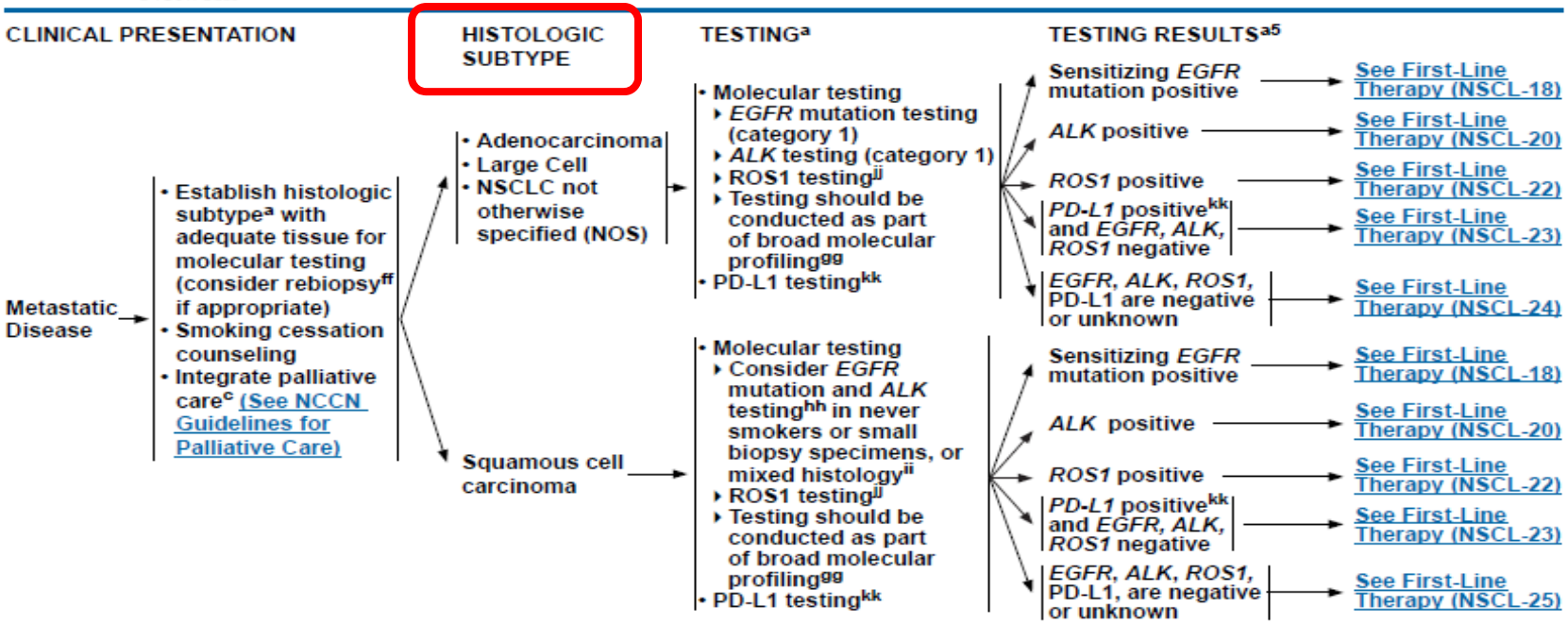
Discussion



[a] See Principles of Pathologic Review (NSCL-A).
[c] Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010;363:733-742.
[ff] If repeat biopsy is not feasible, plasma biopsy should be considered.
[gg] The NCCN NSCLC Guidelines Panel strongly advises broader molecular profiling with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. Broad molecular profiling is a key component of the improvement of care of patients with NSCLC. See Emerging Targeted Agents for Patients With Genetic Alterations (NSCL-H).
[hh] In patients with squamous cell carcinoma, the observed incidence of *EGFR* mutations is 2.7% with a confidence that the true incidence of mutations is less than 3.6%. This frequency of *EGFR* mutations does not justify routine testing of all tumor specimens. Forbes SA, Bharma G, Bamford S, et al. The catalogue of somatic mutations in cancer (COSMIS). Curr Protoc Hum Genet 2008;chapter 10:unit 10.11.
[ii] Paik PK, Varghese AM, Sima CS, et al. Response to erlotinib in patients with *EGFR* mutant advanced non-small cell lung cancers with a squamous or squamous-like component. Mol Cancer Ther 2012;11:2535-2540.
[ij] Shaw AT, Ou S-HI, Bang Y-J, et al. Crizotinib in ROS1-rearranged non-small cell lung cancer. N Engl J Med 2014;371:1963-1971.
[kk] PD-L1 expression levels of ≥50% are a positive test result for first-line pembrolizumab therapy.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

The situation today in Israel

- About 10-15% of lung cancer patients have only cytological prep.
- Thus, the cytology prep pipelines should be compatible with all of the path.\mol path assays.

- The cytology pipelines have been **optimized locally**, but differ from center to center

- ~15 years ago the pathology pipeline was harmonized across the globe (buffered formalin)

The pathology pipeline

- Optimized
- Highly regulated
- And fits all of the present (and future) needs.

- Instead of inventing the wheel.
- Can we use the pathology “wheel”?

What do we need?

- We need a pre-analytical pipeline that is compatible with IHC and molecular assays.
  - Gold standard. Buffered formalin.
- We need our cytological material not to escape the cassette
  - We need to form a mass, interact with formalin (protein based)
  - Preferably compatible with path\mol. path
- Easy, cheap and robust

Plasma-thrombin blocks

- Sections from Plasma-thrombin blocks show better morphological assessment of the malignant cell population and permits immunohistochemsitry.
- **This is the preferred method to prepare cell blocks <u>worldwide</u>.**

https://www.jto.org/article/S1556-0864(15)35114-5/pdf

- The plasma-thrombin method is widely used, and is probably **the most foolproof for general use**. You will need to obtain two ingredients, thrombin and plasma, to perform this method.

1. **Thrombin** can be purchased, and
2. pooled **plasma** can usually be provided by the clinical laboratory.

AMERICAN SOCIETY FOR CYTOTECHNOLOGY
Quality Assessment Center

The steps

- Get the cells in buffered formalin
- Spin, and discard liquid .
- Wash once, Spin and discard liquid
- Add plasma, mix
- Add thrombin, mix
- Let it sit for few minutes at RT

- Transfer the clot to path cassette with sponges.
- Done.

- Has been done at Hadassah for about a year
- Works brilliantly.

- Compatible with all of our present needs.
- Easy, bullet proof.

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- Thank you!