

Tumor Growth Pattern and Intratumoral Fibrosis as Prognostic Factors in Pancreatic Neuroendocrine Neoplasms

Deyali Chatterjee^{1,4}, Gregory Williams^{1,3}, Jingxia Liu^{1,3}, Chet Hammill^{1,3}, William Hawkins^{1,3} and Nikolaos A Trikalinos^{1,2}

²Division of Oncology, Department of Medicine; ³Department of Surgery; ⁴Department of Pathology and Immunology; Washington University in St. Louis, St. Louis, MO.

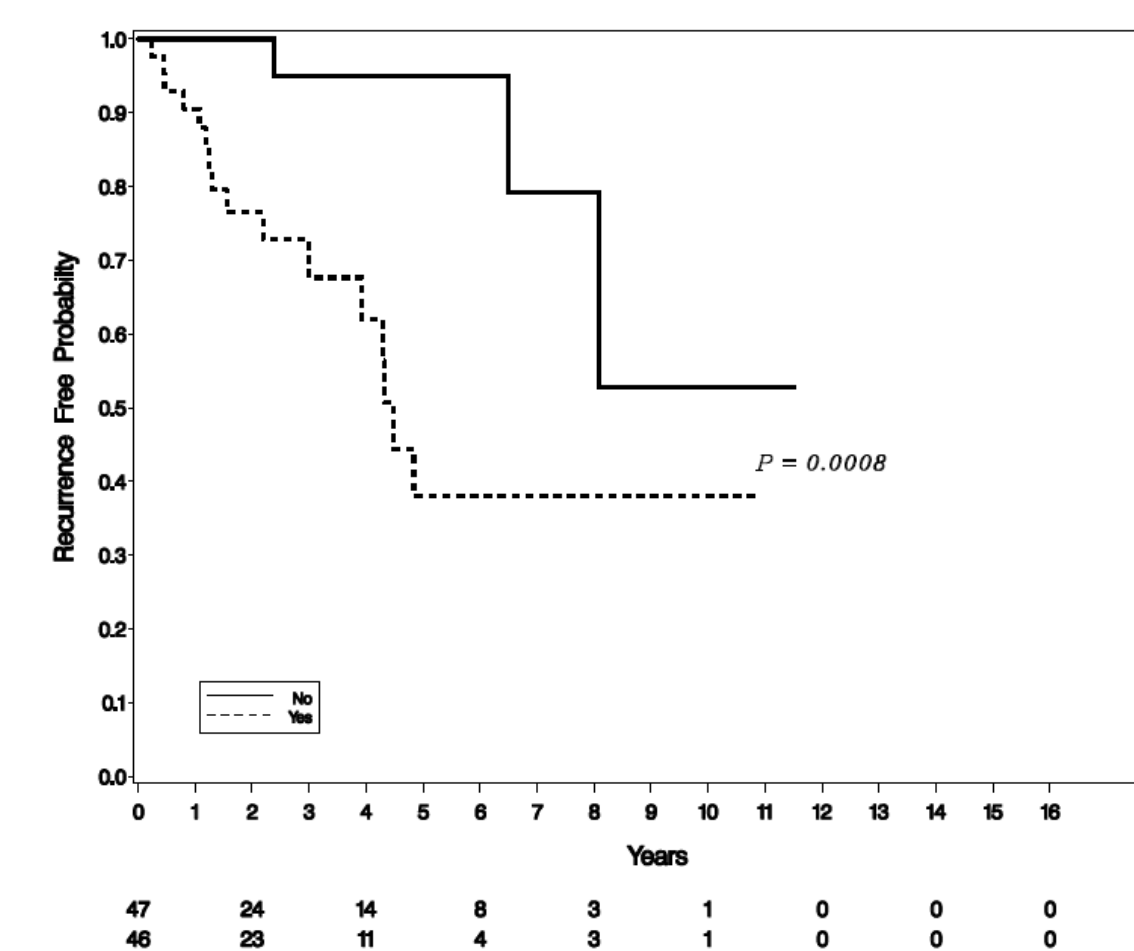
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Introduction

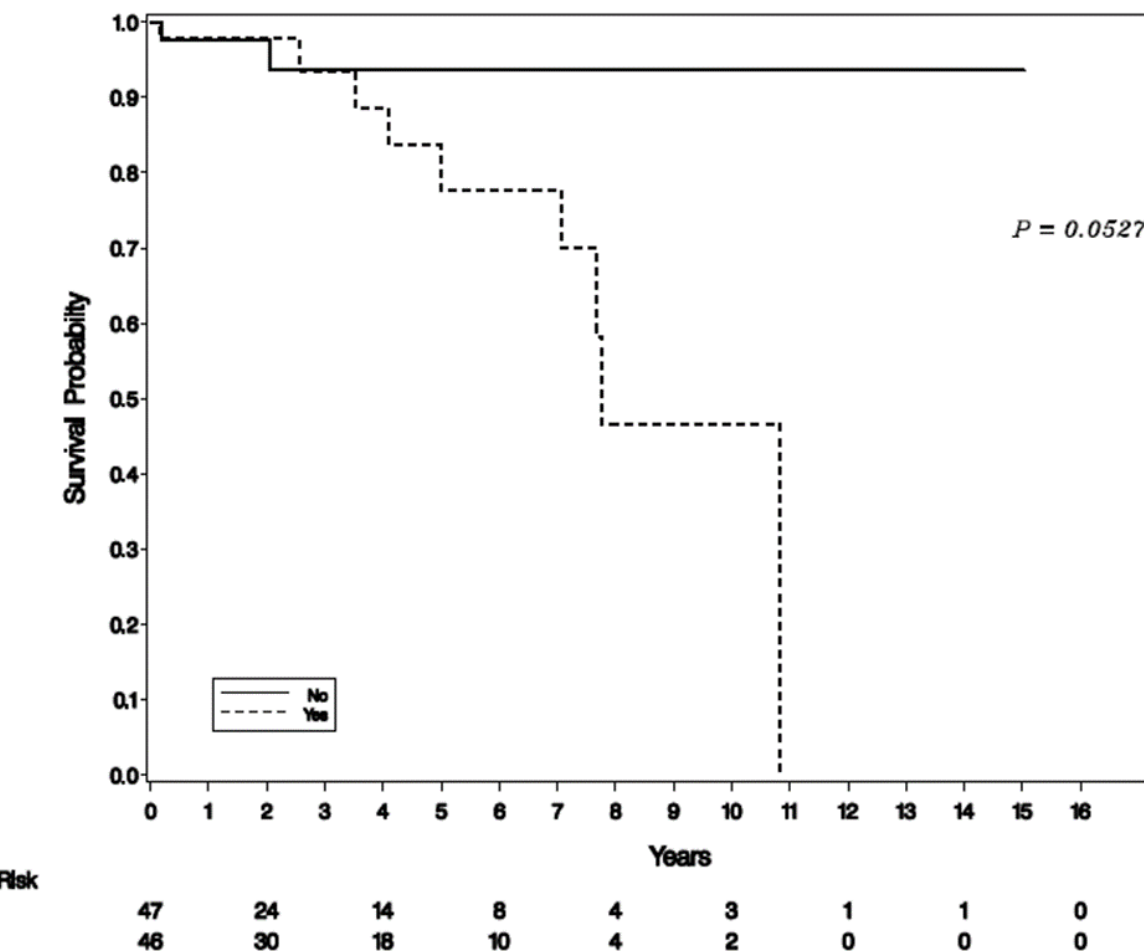
- Established prognostic factors after resection of pancreatic neuroendocrine neoplasms are WHO tumor grade, AJCC tumor stage, molecular characteristics, and other clinicopathologic factors such as status of surgical resection margin, lymph node status, distant metastasis, and lymphovascular invasion.
- Even with established prognostic parameters, the biologic behavior of this group of tumors is still often uncertain, and recurrences are associated with a worse prognosis.
- We hypothesized that other histologic factors such as intratumoral fibrosis and tumor growth patterns may be of prognostic significance.

Methods

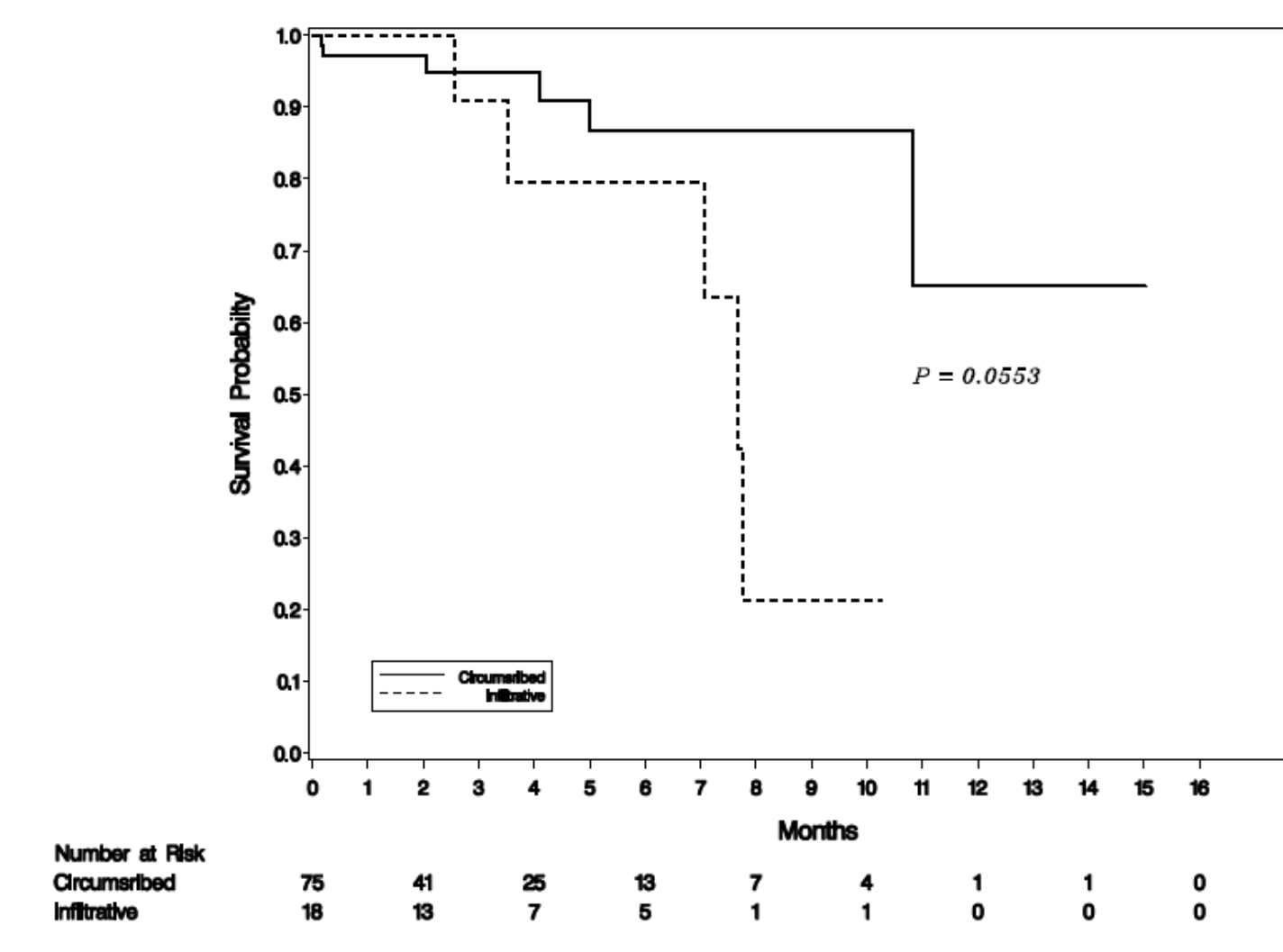
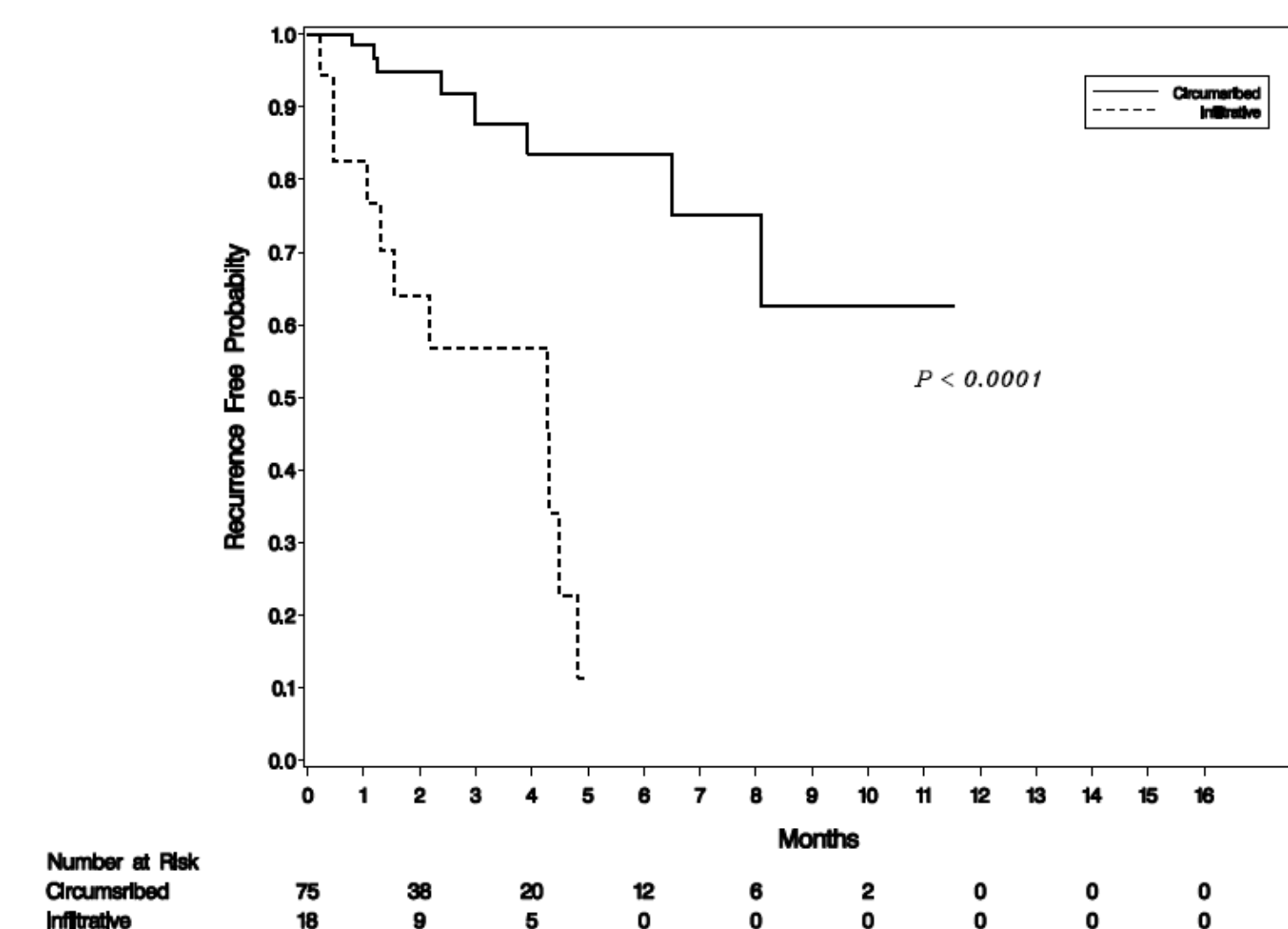
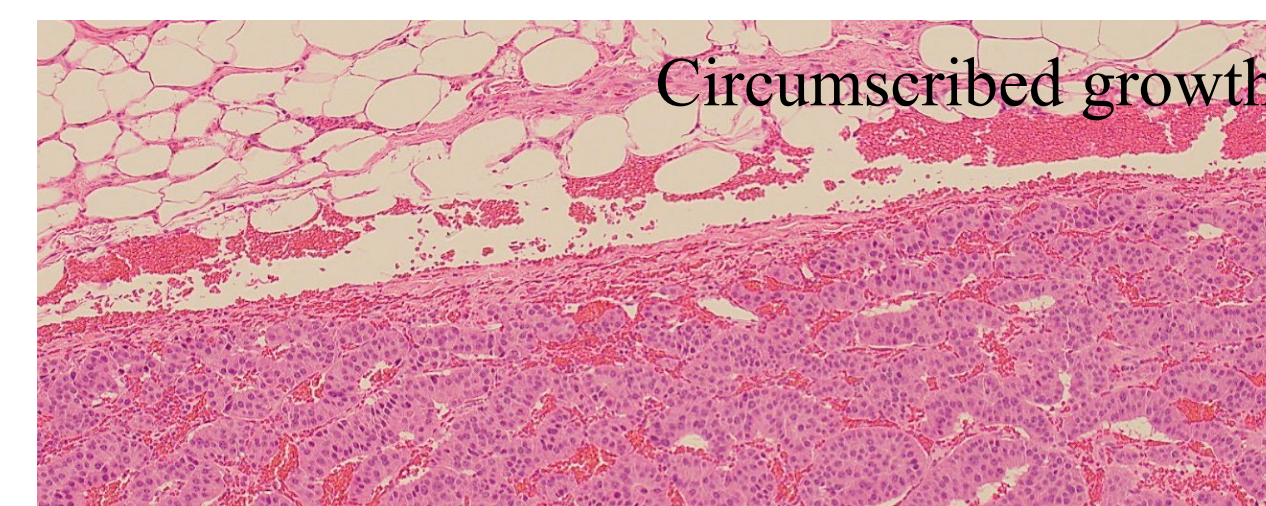
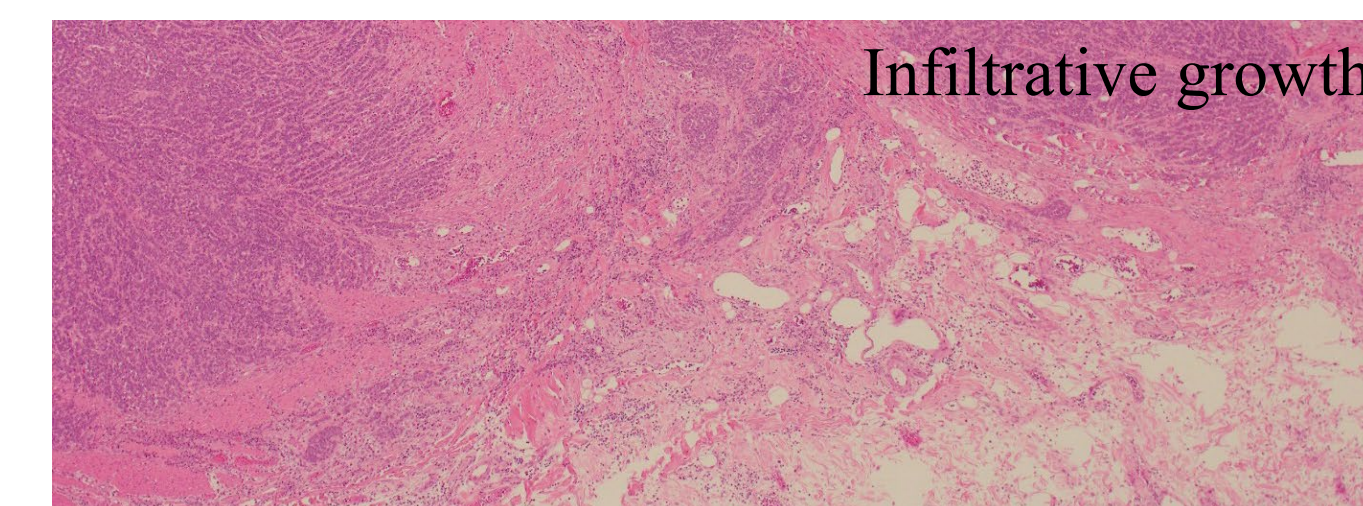
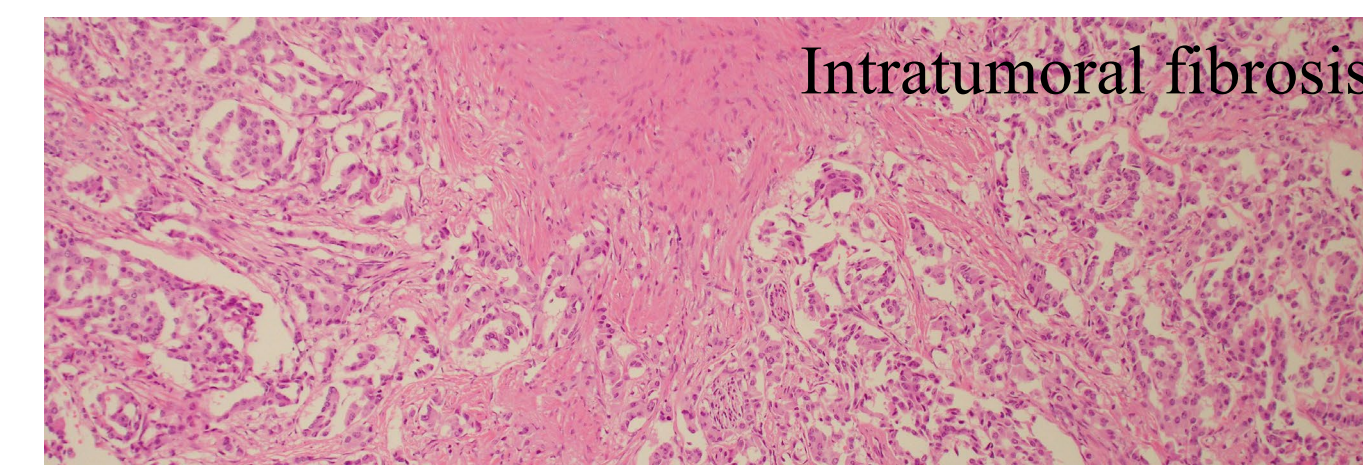
- With institutional IRB approval, we retrospectively evaluated archival pathology slides (2000 – 2017) of definitive resections for PanNEN.
- Follow-up information was obtained from the hospital medical records.
- All the tumors were reclassified based on WHO 2017 grading scheme.
- Additionally, we studied the pattern of tumor growth at the periphery, and accordingly classified them as circumscribed or infiltrative.
- We also noted for the presence of significant intratumoral fibrosis when it covered at least 10% of the entire tumor area examined.
- Kaplan-Meier plots were provided and log-rank test was used to compare the differences of disease free survival (DFS) and overall survival (OS) across the different groups.



Intratumoral fibrosis and survival analysis



Tap figures to enlarge



Tumor growth pattern and survival analysis

Results

- Our cohort comprised 95 patients who underwent definitive resection (60% Whipple, 30% distal pancreatectomy, 5% total pancreatectomy, 4% enucleation, 1% central pancreatectomy) for PanNEN from 2000 and 2017 at our institution.
- Patient demographics: 48 males, 47 females; 88% Caucasian, 10% African American.
- 98% (n=93) cases were well-differentiated NET, 2% (n=2) cases were poorly differentiated NEC.
- There was significant difference in DFS among the different WHO grades ($p < 0.0001$), confirming the validity of the classification in this cohort.
- 49.5% (n=47) cases had intratumoral fibrosis
- 80% (n=76) cases had a circumscribed growth pattern
- Cases with fibrosis had a circumscribed growth pattern in 62.5%, as compared to those with no fibrosis (98%; $p < 0.001$)
- Cases of intratumoral fibrosis had a significantly increased association with other prognostic factors such as lymphovascular invasion ($p = 0.0005$), perineural invasion ($p = 0.0121$), Ki-67 index ($p = 0.003$) and lymph node positivity ($p = 0.002$)
- Additionally, PanNEN with intratumoral fibrosis showed significantly reduced DFS ($p = 0.0008$) and OS ($p = 0.05$)
- Likewise, PanNEN with an infiltrative growth pattern showed significantly reduced DFS ($p < 0.0001$) and OS ($p = 0.05$)

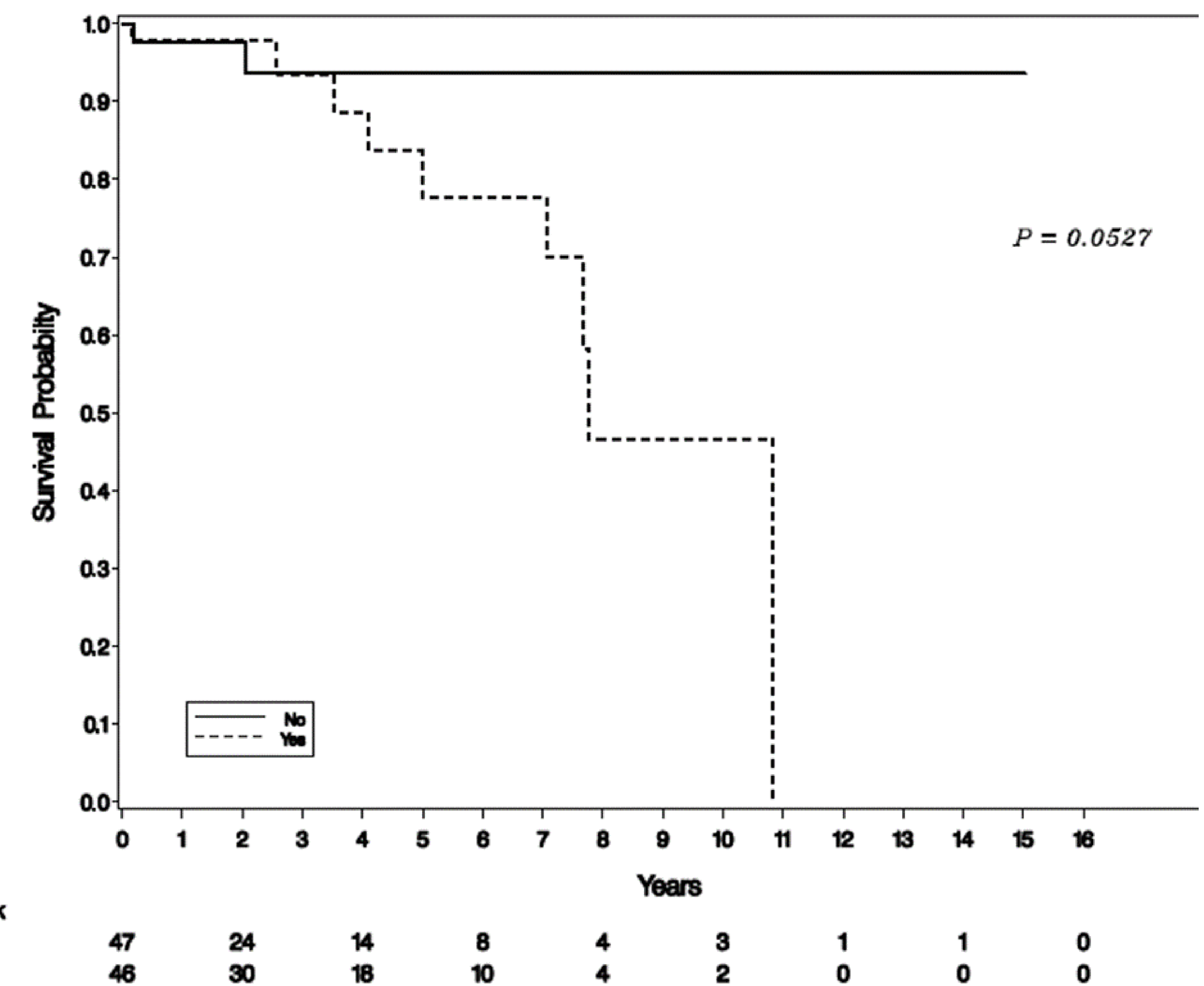
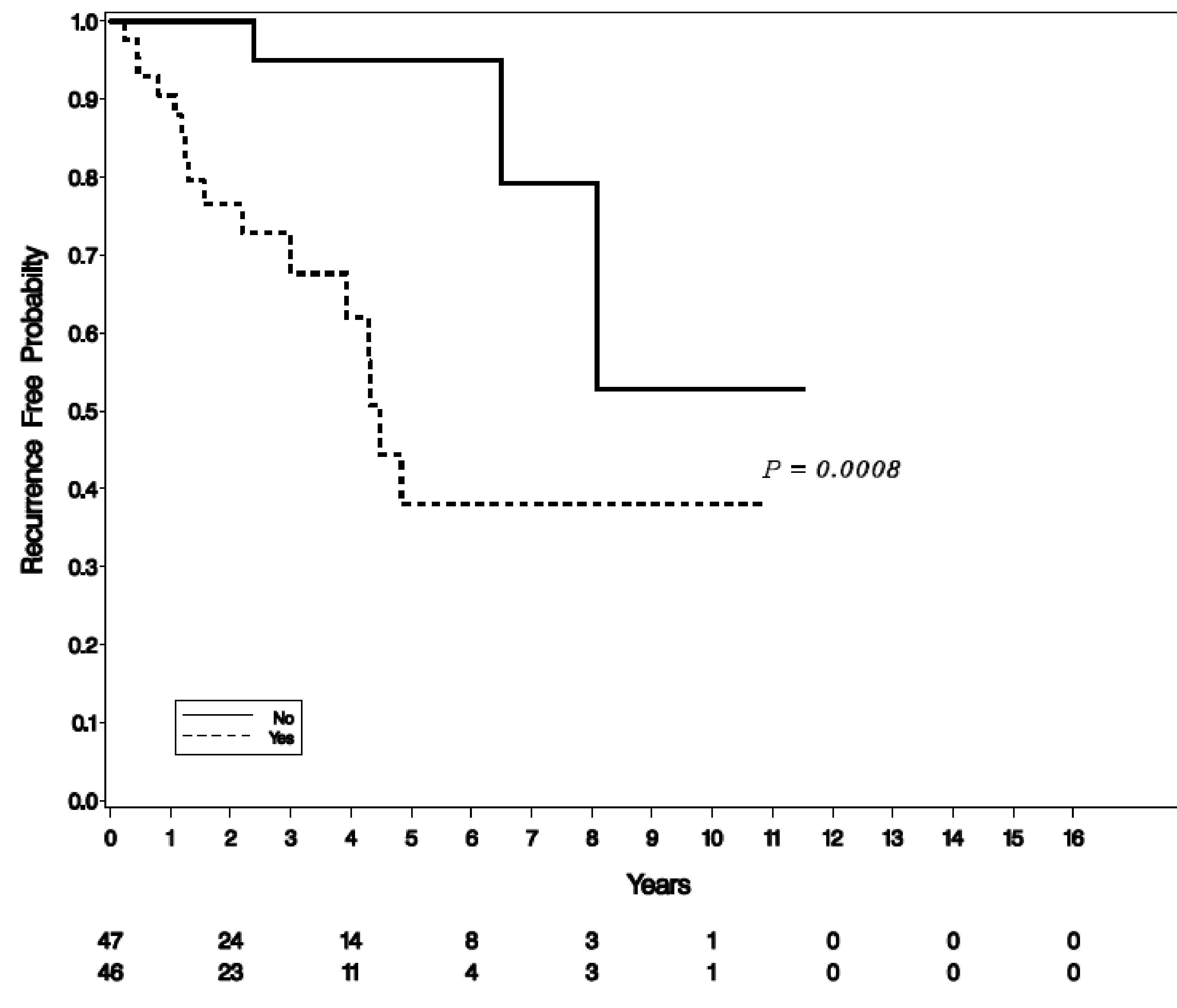
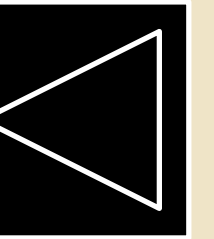
Conclusions

- This is the first study to show the prognostic significance of tumor growth pattern (circumscribed versus infiltrative).
- This study also validates the prognostic significance of intratumoral fibrosis in PanNEN.

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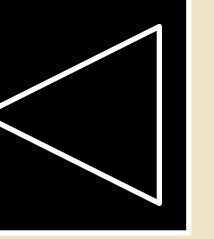


Intratumoral fibrosis and survival analysis

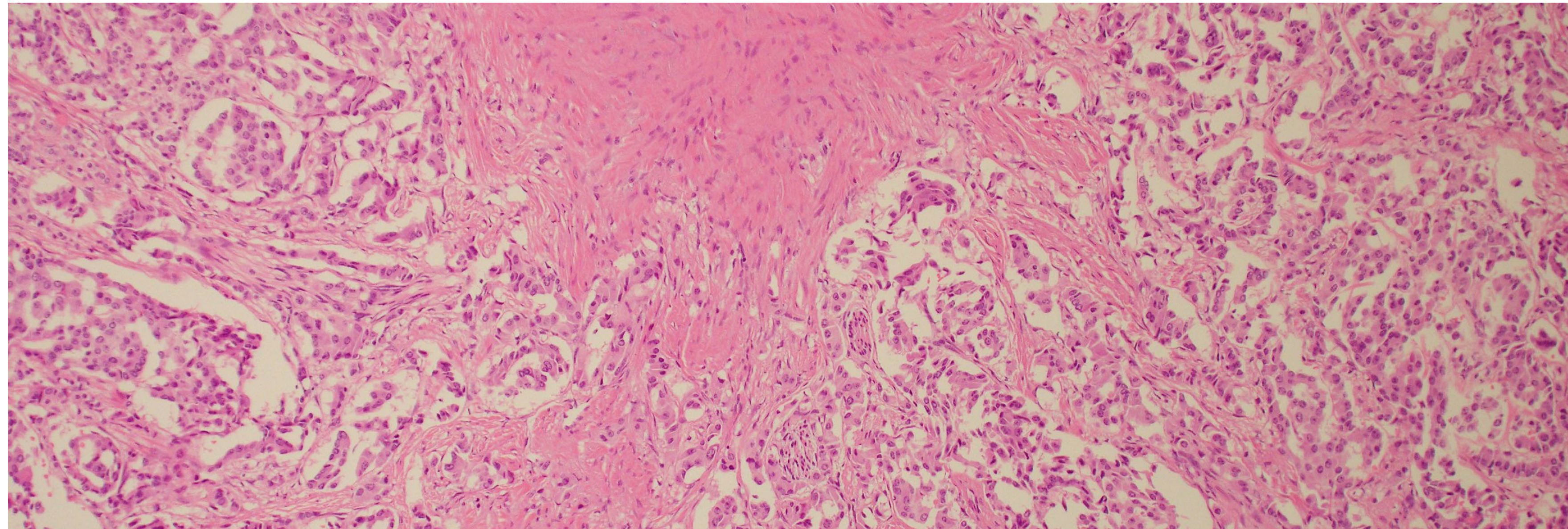
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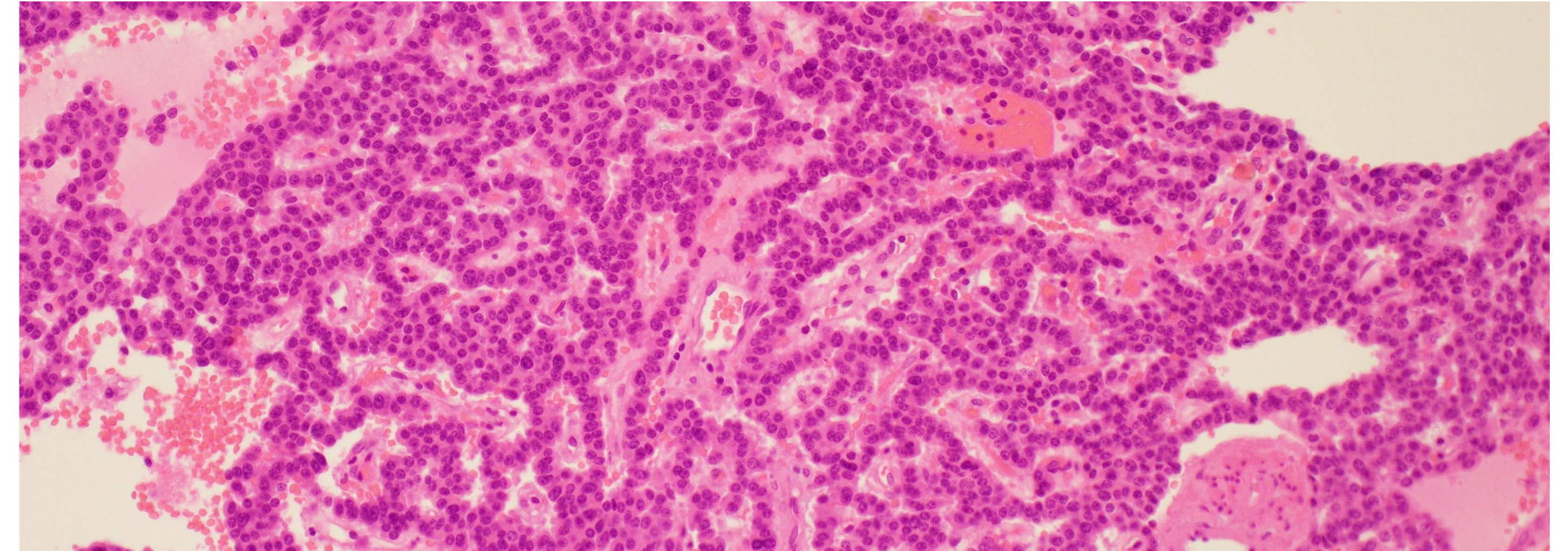
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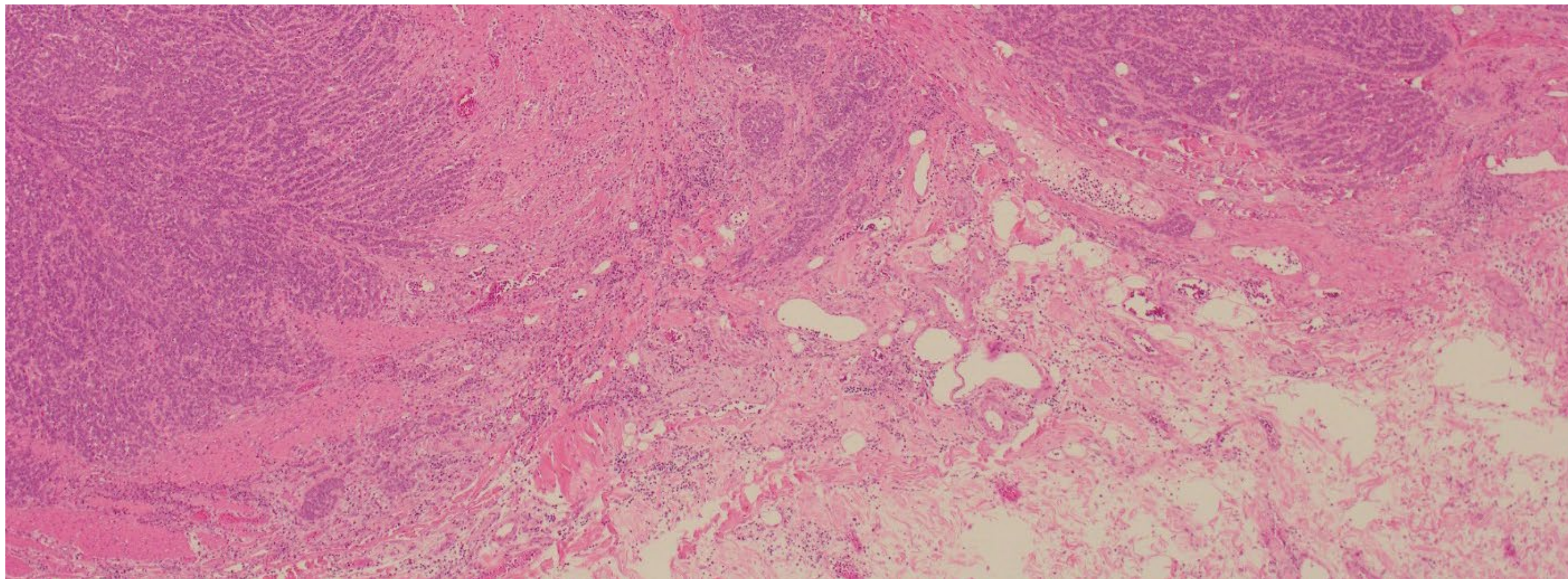
Intratumoral fibrosis



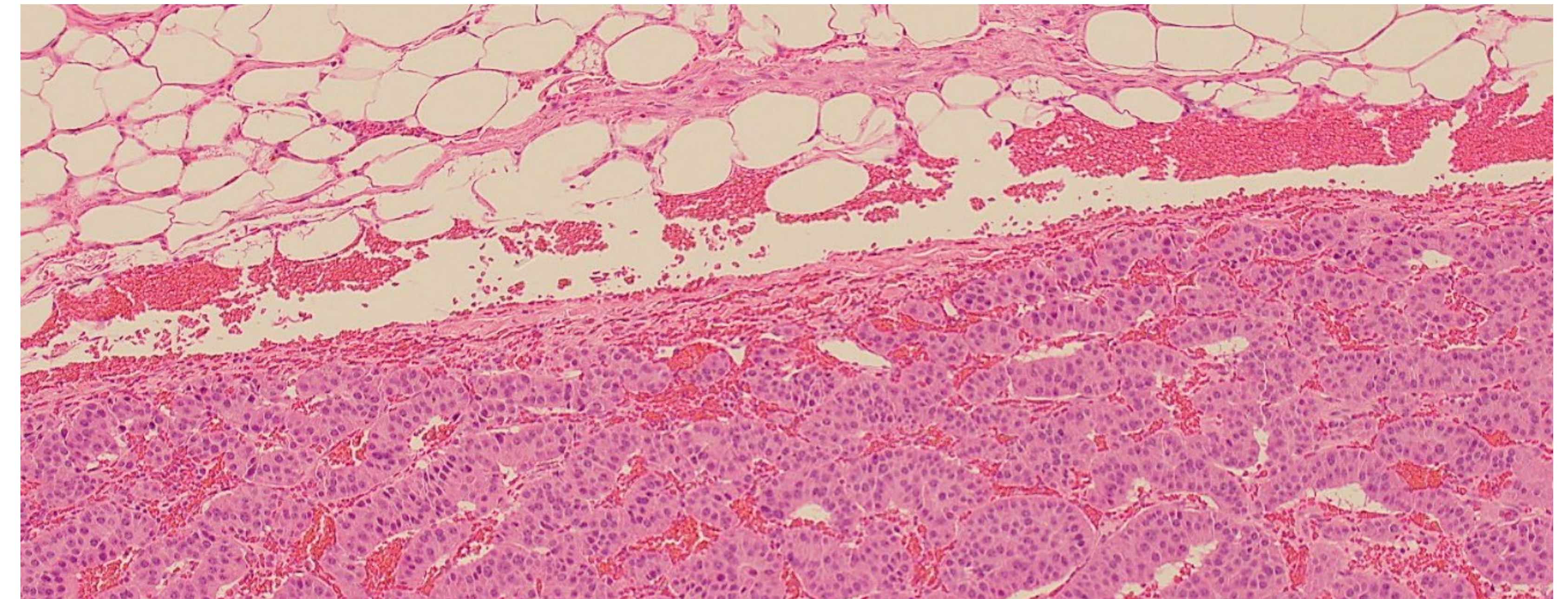
No intratumoral fibrosis



Infiltrative growth



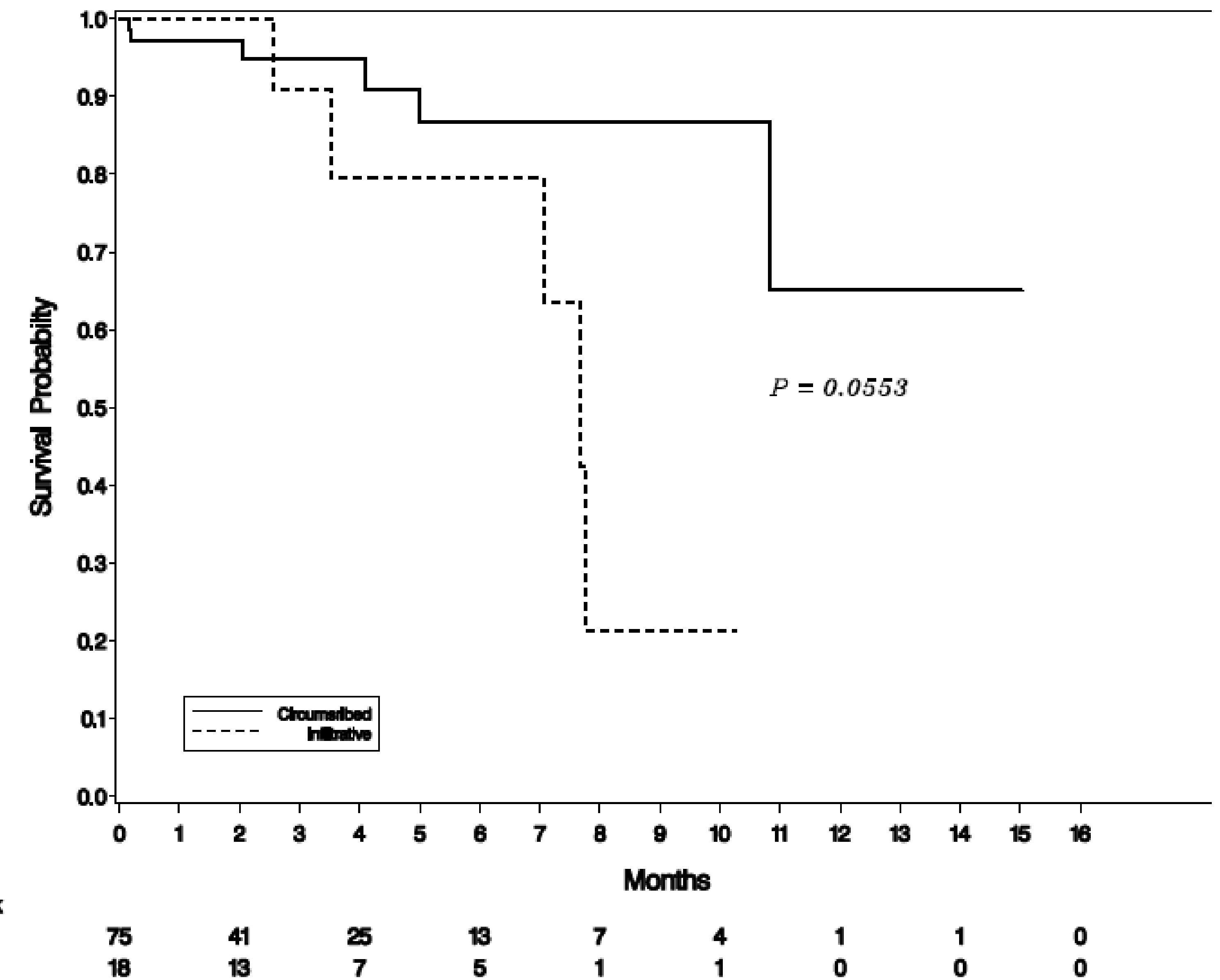
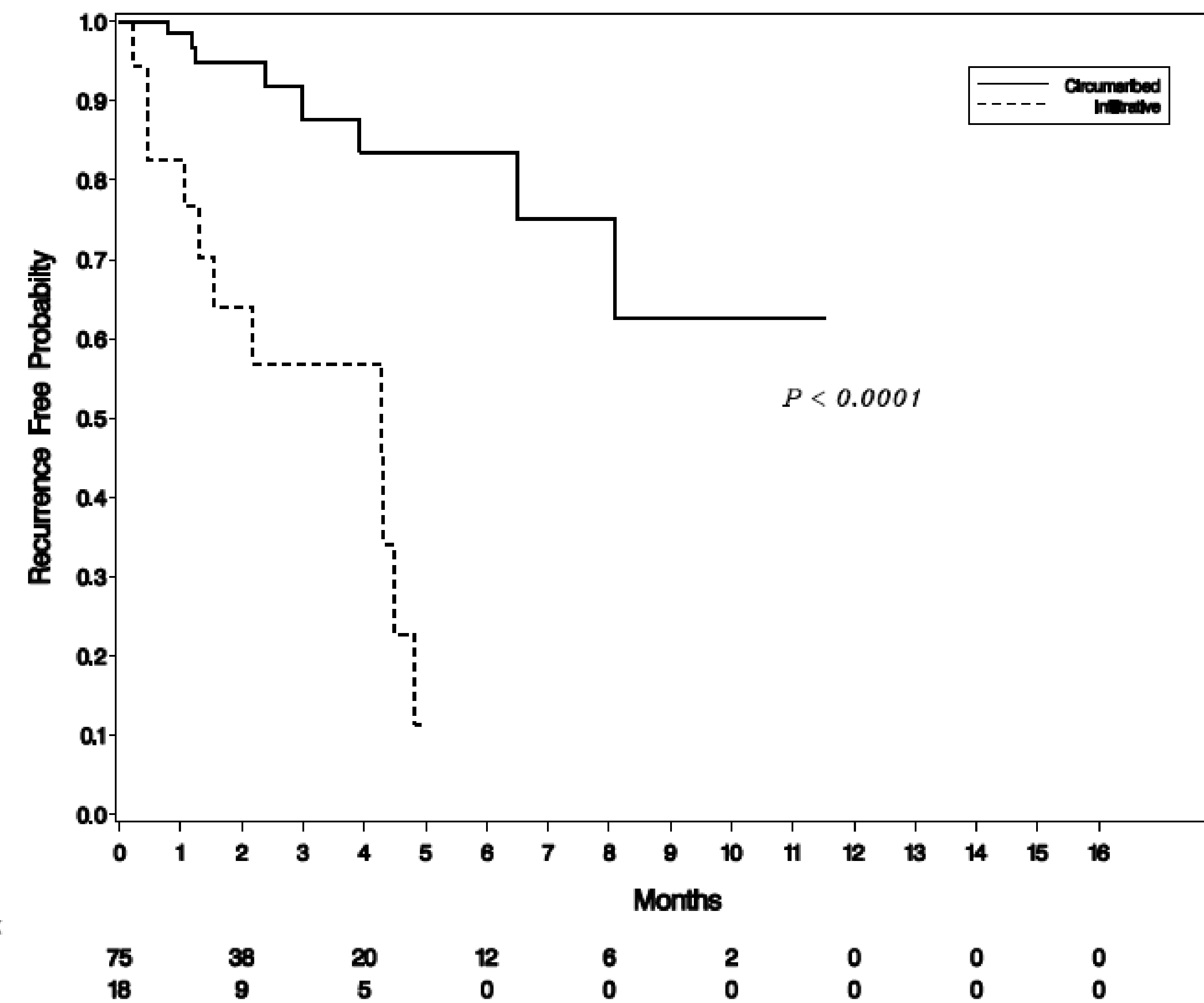
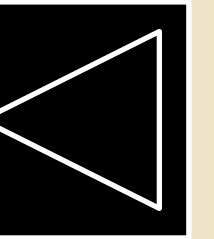
Circumscribed growth



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