

Time to administration of stereotactic radiosurgery to the cavity after surgery for brain metastases. A real-world analysis.

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OBJECTIVES

- Assess real-world LR for BM pts referred for SRS
- Identify predictors of SRS timing

BACKGROUND

- For single/sx BMs, surgery ↓ sx, ↑ LC, ↑ independence, ↑ OS¹
 - Resection alone → ~50% LC^{1,2}
- Adjuvant RT ↑ LC (73-90%), ↓ new BMs, ↓ neuro death¹⁻³
- Adjuvant SRS not delivered immediately, to allow for healing & cavity shrinkage/stabilization
- With ↑ time surgery → SRS, risk of tumor repopulation
- **No consensus on optimal adjuvant SRS timing!**
- Often, only outcomes of pts w timely SRS reported → **Actual efficacy likely lower than reported!**
- Subset of pts never receive SRS for variety of reasons
- **Etiology of interval to SRS, its causes & impact on LC not well understood**

¹ Patchell et al. *N Engl J Med.* 1990; ² Patchell RA et al. *JAMA.* 1998; ³ Kocher et al. *J Clin Oncol.* 2011.

METHODS

Patient Selection

- Retrospectively reviewed path records, 2012-2018
- **Eligibility criteria:**
 - Adults
 - Path-confirmed BM from solid tumor
 - Surgically resected
 - Referred for adjuvant SRS
 - ≥1 mo f/u
 - No prior localized tx (surgery, SRS, brachy)

SRS

- LINAC: Varian iX w X-Knife or Novalis Truebeam w ExacTrac
- Immobilization: Frame-based or thermoplastic mask
- Thin-slice, volumetric T1+C MRI brain sequences co-registered
- Treatment planning: BrainLab
- CTV = resection cavity + contrast enhancement; PTV = CTV + 2 mm
- Dose: 18-33 Gy (median 24 Gy) in 1-5 fx
 - Prescribed to 80% isodose line

Endpoints

- **1^o endpoint: time to adjuvant SRS**
 - 1) ≤4 weeks postop
 - 2) >4-8 weeks postop
 - 3) >8 weeks postop
 - 4) Not completed
- **2^o endpoints:** LR, LRFS, OS, **causes of intervals surgery → SRS**

RESULTS

- **Time to SRS only predictor of LR (p<0.01)**
- **↑ LR & ↓ LRFS w time to SRS (p<0.01)** (Fig. 1 & 2)
- **Predictive of ↑ time to SRS**
 - **NSCLC (p=0.04)**
 - **Earlier yr of tx (p<0.01)** (Fig. 3)
- **Causes of time to adjuvant SRS >4 weeks** (Fig. 4)
 - **Logistics**
 - **Mgmt of 1^o or systemic disease**
 - **Mgmt of pre-existing conditions**

Table 1: Demographic, disease & treatment characteristics, by time to adjuvant SRS

| | All (n=159) | ≤4 weeks (n=44) | >4-8 weeks (n=62) | >8 weeks / no SRS (n=53) | p-value |
|----------------------------------|-------------------|-------------------|-------------------|--------------------------|---------------------|
| Demographics | | | | | |
| Age, yrs, (median, IQR) | 64.0 (55.0, 70.0) | 62.5 (55.0, 70.0) | 64.5 (52.3, 69.0) | 65 (56.0, 70.0) | 0.88 ^a |
| Gender (n, %) | | | | | 0.54 ^b |
| Male | 69 (43.4) | 16 (35.4) | 29 (46.8) | 24 (45.3) | |
| Female | 90 (56.6) | 28 (63.6) | 33 (53.2) | 29 (54.7) | |
| Race (n, %) | | | | | 0.07 ^b |
| White | 69 (43.4) | 24 (54.4) | 26 (41.9) | 19 (35.8) | |
| Non-white | 21 (13.2) | 6 (13.6) | 7 (11.3) | 8 (15.1) | |
| RPA (n, %) | | | | | 0.42 ^b |
| I | 28 (17.6) | 8 (18.2) | 8 (12.9) | 12 (22.6) | |
| II | 91 (57.2) | 26 (59.1) | 40 (64.5) | 25 (47.2) | |
| III | 40 (25.2) | 10 (22.7) | 14 (22.6) | 16 (30.2) | |
| Disease characteristics | | | | | |
| Size, cm (median, IQR) | 2.9 (2.5, 3.8) | 3.0 (2.7-3.9) | 2.8 (2.5-3.7) | 2.9 (2.5-3.9) | 0.54 ^a |
| Pathology (n, %) | | | | | 0.04 ^{b,d} |
| NSCLC | 69 (43.4) | 16 (36.4) | 23 (37.1) | 30 (56.6) | |
| Other | 90 (56.6) | 28 (63.6) | 39 (62.9) | 23 (43.4) | |
| Add'l BM (n, %) | 77 (48.4) | 19 (43.2) | 29 (46.7) | 29 (54.7) | 0.25 ^b |
| Active syst dz (n, %) | 111 (69.8) | 32 (72.7) | 41 (66.1) | 38 (71.7) | 0.95 ^b |
| Treatment characteristics | | | | | |
| Yr of tx (n, %) | | | | | <0.01 ^b |
| 2012-2014 | 47 (29.6) | 7 (15.9) | 16 (25.8) | 24 (45.3) | |
| 2015-2016 | 47 (29.6) | 10 (22.7) | 22 (35.5) | 15 (28.3) | |
| 2017-2018 | 65 (40.9) | 27 (61.4) | 24 (38.7) | 14 (26.4) | |
| GTR (n, %) | 132 (83.0) | 34 (77.3) | 54 (87.1) | 44 (83.0) | 0.49 ^b |
| RT Fx & Dose (n, %) | | | | | 0.92 ^b |
| 1 fx (18-20 Gy) | 10 (7.2) | 2 (4.5) | 5 (8.1) | 3 (9.4) | |
| 3 fx (24-33 Gy) | 69 (49.6) | 22 (50.0) | 32 (51.6) | 15 (46.9) | |
| 5 fx (25-30 Gy) | 59 (42.4) | 20 (45.5) | 25 (40.3) | 14 (43.8) | |
| Syst tx postop (n, %) | 104 (65.4) | 28 (63.6) | 48 (77.4) | 28 (52.8) | 0.02 ^b |

^a Kruskal-Wallis test; ^b Chi-square test or chi-square test for trend; ^c Cerebellar location vs. other; ^d NSCLC versus other pathology.

CONCLUSION

- For resected BM, ↑ LR w ↑ time surgery → SRS
- NSCLC pathology & earlier yr of tx associated w ↑ time surgery → SRS
- Causes of ↑ interval to SRS: logistics, mgmt of 1^o & systemic dz, mgmt of comorbidities
- Opportunity to ↑ LC w improvements in workflow, multidisciplinary mgmt

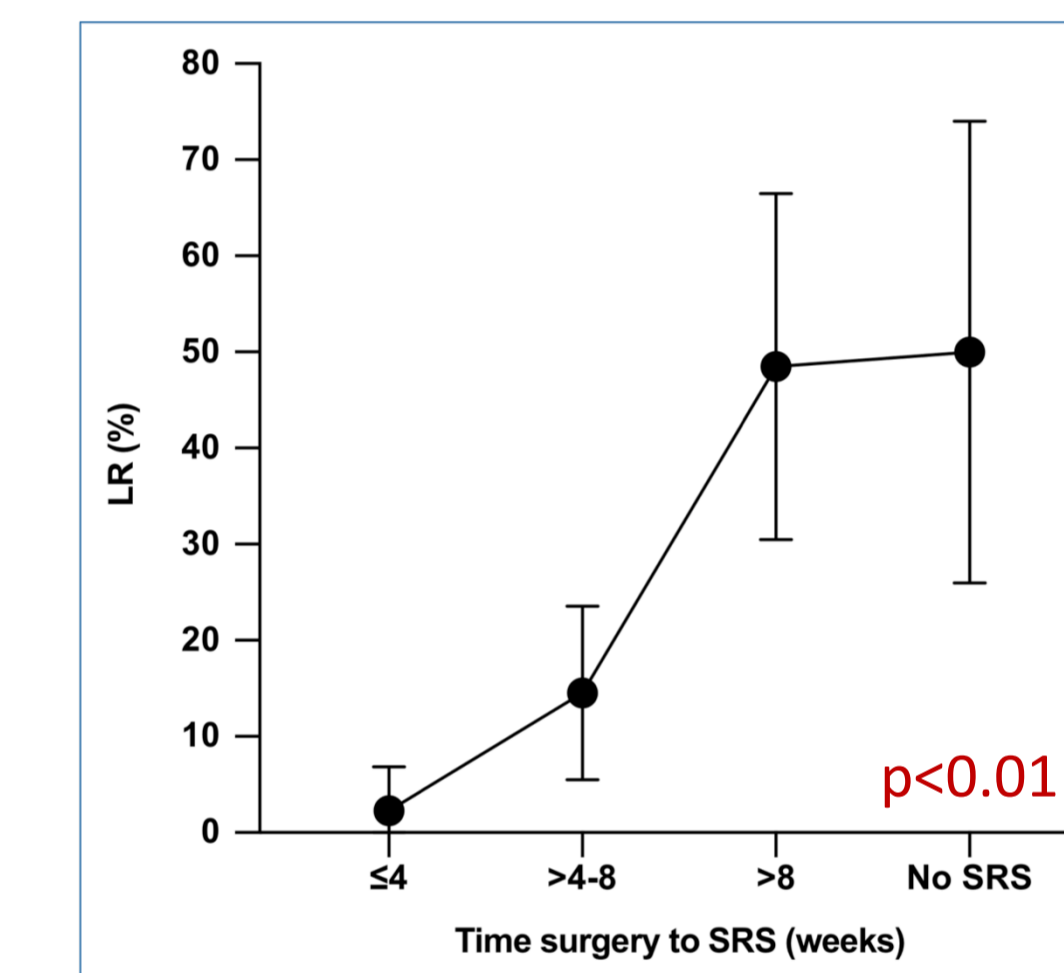


Fig. 1: LR by time to SRS (95% CI)

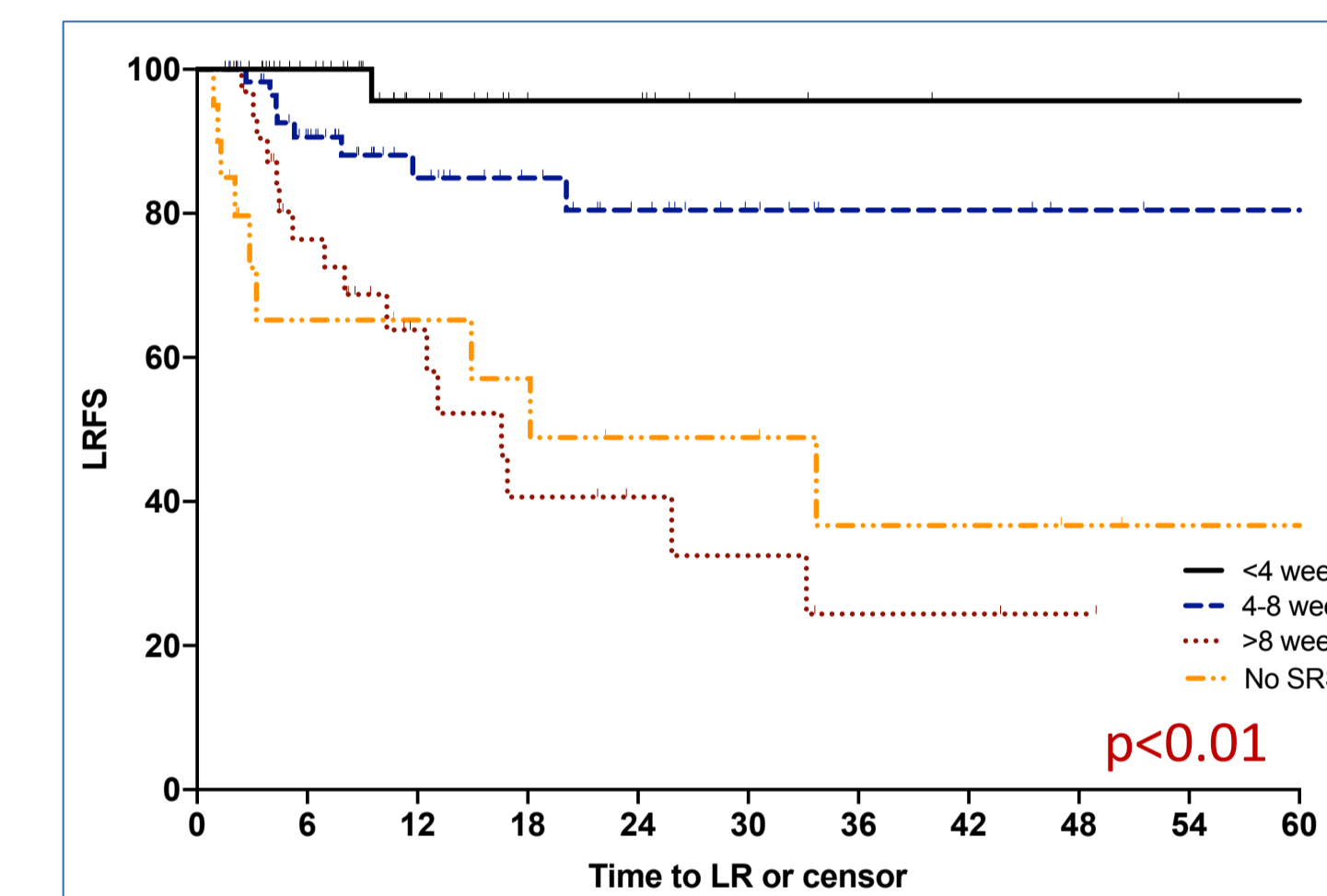


Fig. 2: LRFS by time to SRS

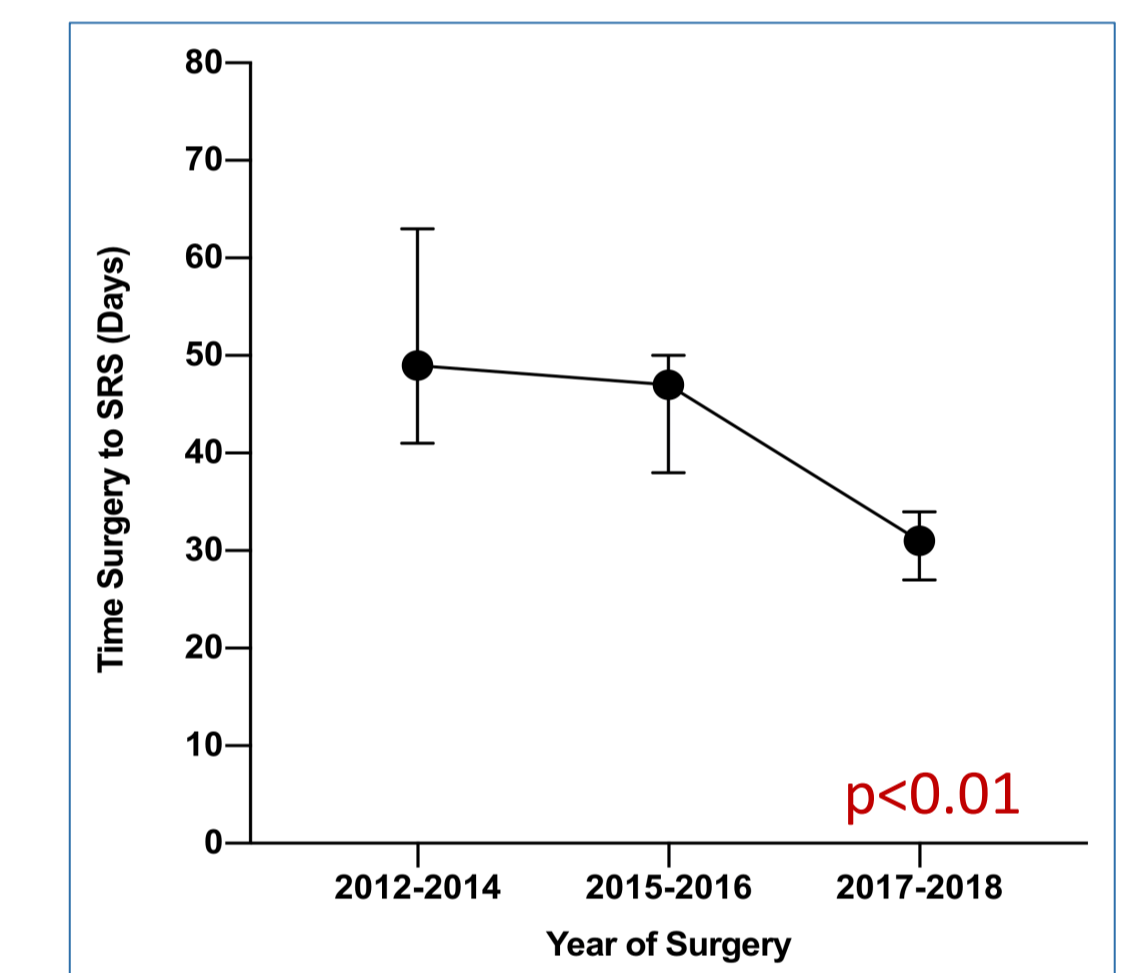


Fig. 3: Time surgery → SRS by yr

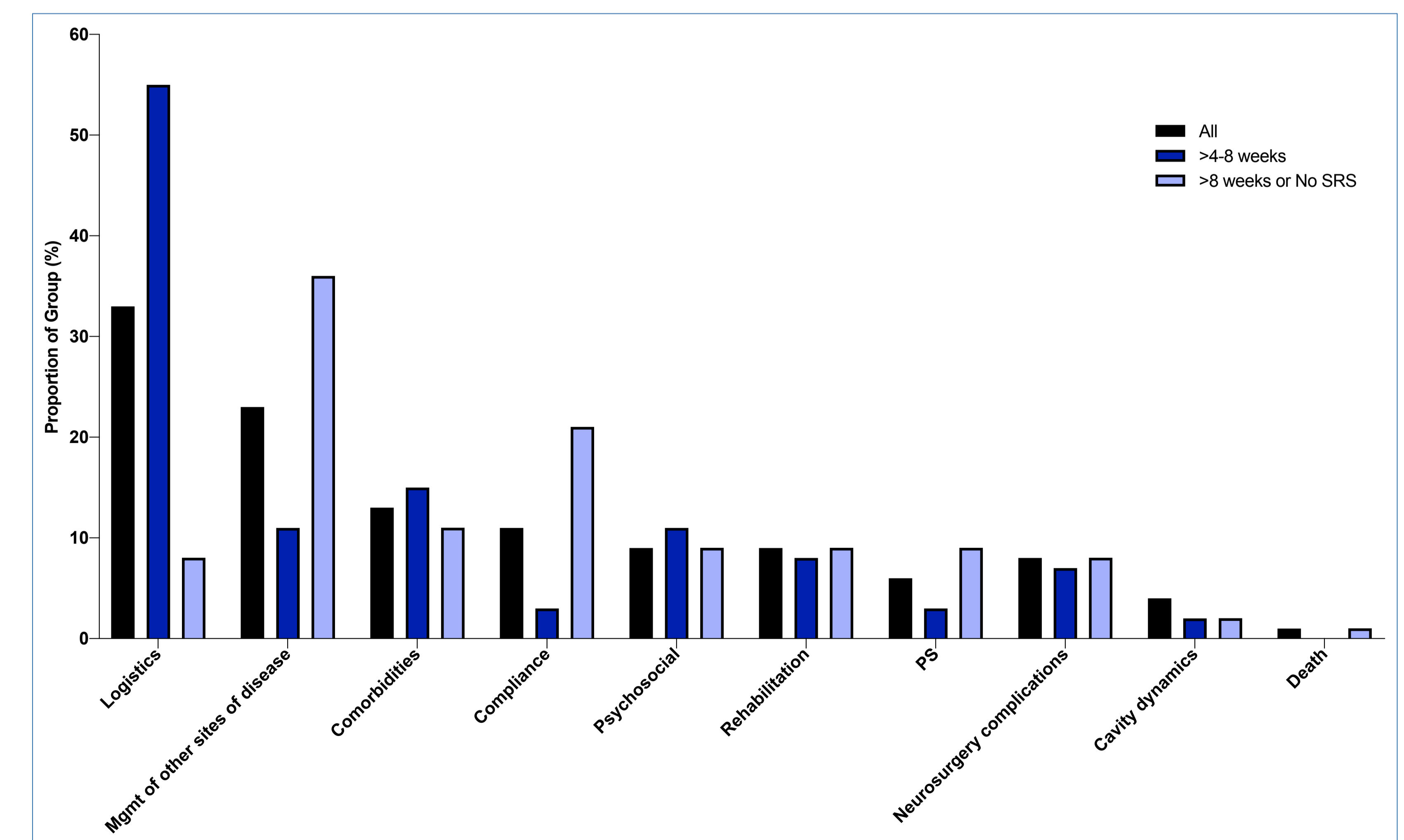


Fig 4: Causes of interval to SRS >4 weeks postop