ADHESIVE SEALANT BIOMATERIALS

Clinical Series

David Mandley PhD
Tissuemed Ltd.

Evaluation of a novel Adhesive Film for sealing Air Leaks after Lung Surgery

Summary

This paper presents the findings of twenty patients treated with TissuePatch™3 (TP3), a novel synthetic surgical sealant film as an adjunct in the management of parenchymal air leaks following lung resection. The surgery took place in two thoracic centres in the United Kingdom; St James's University Hospital, Leeds and Norfolk and Norwich Hospital (N&N). Preliminary results revealed that TP3 eliminated air leaks at the point of chest closure, 12 out of the 15 subjects (80%) being air leak free at the end of the surgical procedure and reduced the time to the last recorded air leak when compared to control patients (statistically significant for patients treated at the N&N centre). There were no device related adverse events with an overall high degree satisfaction from operators.

Background

Air leaks in lung surgery pose a hazard for thoracic surgical patients[1-3] and can lead to complications with prolonged chest drain presence and hospital stay. This preliminary study was designed to investigate the intraoperative and post-operative performance of a new synthetic sealant film, TP3 (Tissuemed Ltd). The product was designed to offer effective sealing of air leaks in a user-friendly presentation including minimum foreign body application, rapid delivery to operating field, zero preparation time and very short application time. The study forms part of Tissuemed's obligations to provide post marketing surveillance data for regulatory purposes.

Methods

Patients were recruited between May 2007 and September 2007 at two centres, and by one Consultant Thoracic Surgeon at each centre, as follows; St James's University Teaching Hospital in Leeds (Mr K Papagiannopoulos) and Norfolk and Norwich Hospital (Mr W Parry).

Patients eligible for entry into the study were those undergoing elective lung resection by open thoracotomy. Patient selection was based on the presence of an air leak following resection of grade 2 or less. Grade 3 leaks were reduced to maximum grade 2 with sutures prior to application of the patch. Air leaks were graded 1, 2 or 3 according to a well defined grading system[4]. All patients in the study group were followed up at 3 months post operatively.

The clinicians at both centres were asked to express their level of satisfaction with a) TP3 application and b) the overall procedure. The surgeons were asked to score as follows; extremely satisfied, moderately satisfied, moderately dissatisfied or extremely dissatisfied.

The clinicians at both centres provided retrospective control data[5] from a comparable patient population.

The study was managed and independently monitored by Medvance Ltd.

Results

Study Population / Demographic Data

20 patients were recruited into this study, five of whom were older than 75, outside the inclusion criteria. Of those patients included in the study there were 11 (73%) male and 4 (27%) female subjects. Age ranged from 49 to 75 (SD 8.2) with a mean value of 64.8.

Of the 15 patients included in this data analysis, there were 13 lobectomies performed and 2 wedge resections. A total of 21 air leaks were treated. 11 subjects had 1 air leak, 2 subjects had 2 air leaks and 2 subjects had 3 air leaks prior to treatment with TP3. All seven of the patients from the Norfolk and Norwich centre had one air leak only.

Seven (33.3%) of the 21 total air leaks were Grade 2 and 14 (66.6%) were Grade 1. All seven Norfolk and Norwich patients' air leaks were grade 2. For the eight patients at St James's (yielding a total of 14 air leaks), all were grade 1.

In summary, air leaks treated by the clinician at the Norfolk and Norwich were consistently scored as grade 2, a higher grading than the grade 1 air leaks treated at St James's in Leeds.

Air Leak reduction at chest closure

Twelve of the 15 treated subjects had no remaining air leaks at chest closure (80%). For the rest of the group maximum time to the last air leak being present was 120 hours and the minimum 0. All the patients in the control group had recorded air leaks following chest closure. The maximum time to the last air leak present was 120 hours and the minimum 0 hours.

Manufactured by: Tissuemed Ltd.•5 Killingbeck Drive•Leeds•LS14 6UK•United Kingdom
www.tissuemed.com•Tel +44(0)1132000500•Fax +44(0)1132407343•

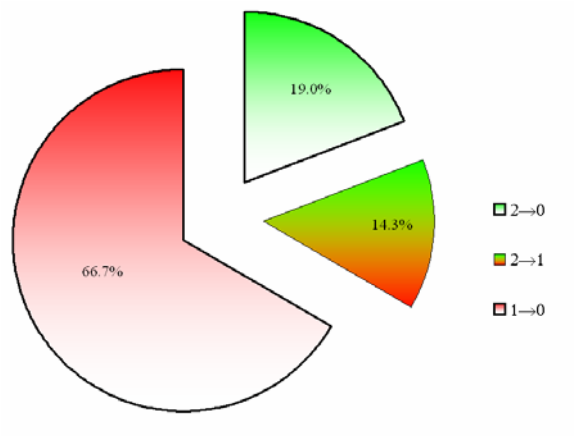


Figure 1 Breakdown of change in air leak grades, pre-post TP3 treatment

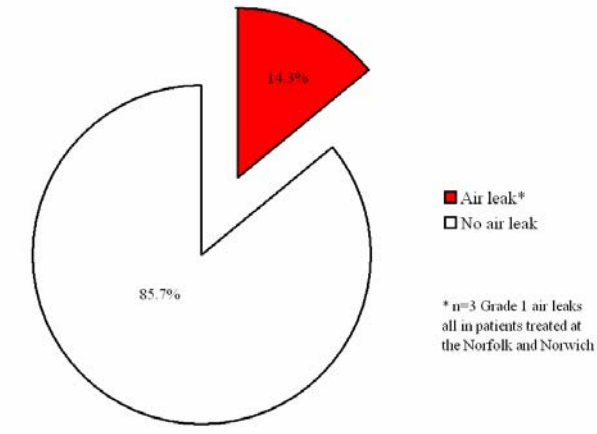


Figure 2 Breakdown of the post-treatment air leak grades (as a % of number of air leaks)

Time to last air leak recorded

At both centres, **'**time to the last air leak recorded' was shorter for the 15 patients treated with TP3. This was statistically significant at Norfolk and Norwich (p=0.05). For the patients treated at Leeds, whilst the average time to the last air leak recorded was lower (49.8 c.f 59.3 hours) there was no statistically significant difference between control and TP3 treated patients.

Table 1 Time to last air leak (hours)

	Leeds Treated	**Leeds Control**	**N&N Treated**	**N&N Control**
Mean	**49.8**	**59.3**	**12**	**69.6**
Median	**48**	**48**	**0**	**72**
Min-Max	**0-120**	**0-120**	**0-72**	**48-96**
N^{o} Patients	8	10	7	10

Time to chest drain removal

For patients treated with TP3 at the Norfolk and Norwich Hospital, despite the significant reduction in the **'**time to the last air leak recorded', this was not reflected in the time to chest drain removal, with the mean time to drain removal for treated or control patients being 5 to 6 days. The median time to drain removal of TissuePatch3 treated patients was lower than the control group, 3 c.f 5 days. In Leeds, both the mean and median times for chest drain removal of TissuePatch3 treated cases were shorter than the control subjects. Again the combination of low patient numbers with a wide range of data means that these results were indicative only with no statistical significance (p=0.05).

Table 2 Time to chest drain removal (days)

	Leeds Treated	**Leeds Control**	**N&N Treated**	**N&N Control**
Mean	**9.4**	**14.1**	**5.4**	**5.5**
Median	**9**	**11.5**	**3**	**5**
Min-Max	**2-21**	**3-54**	**1-23**	**3-8**
N^{o} Patients	8	10	7	10

Time to discharge

For TissuePatch3 patients treated at the Norfolk and Norwich hospital, despite the significant reduction in the **'**time to the last air leak recorded', this was not reflected in the time to hospital discharge. In Leeds, both the mean and median times for hospital discharge of TissuePatch3 treated cases were shorter (each by 2 days) than the control subjects. Once again, due to the low patient numbers and the range of data presented, analysis by Mann-Whitney (considering each centre in isolation) revealed no statistical difference (p=0.05) between control and TissuePatch3 treated cases.

Clinician satisfaction

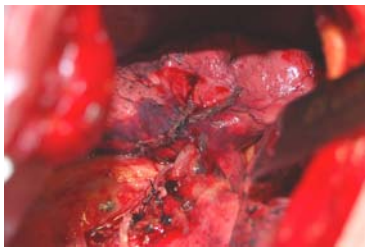
During the course of this post market study, both clinicians were consistently (100%) extremely satisfied with TissuePatch3 application. Overall surgical procedure satisfaction level showed 87% of the procedures being scored as extremely satisfactory and the remainder moderately satisfactory.

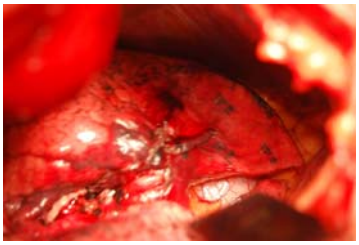
Adverse events

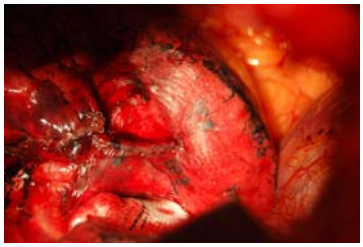
There have been no device-related or non-serious adverse events reported to date. One death occurred in the study as a result of patient co-morbidities.

Manufactured by: Tissuemed Ltd.•5 Killingbeck Drive•Leeds•LS14 6UK•United Kingdom
www.tissuemed.com•Tel +44(0)1132000500•Fax +44(0)1132407343•

Images show resection site with no patch applied, patch applied and finally patch applied, lung inflated







Conclusions

This two-centre post market study involved the use of TP3 as an adjunct in the prevention of air leaks during thoracic surgery. The study has revealed that in this patient population the product:

- eliminated air leaks at chest closure
- reduced the time to the last recorded air leak when compared to control patients. (statistically significant for patients treated at the Norfolk and Norwich centre).
- resulted in 12 out of the 15 subjects (80%) being air leak free at the end of the surgical procedure.
- provided a high degree of surgeon satisfaction
- was associated with no device related adverse events

Are there financial benefits when sealants are used in lung surgery?
Analysis of the data in this study suggests that the effective reduction of air leaks using an intraoperative sealant film has the *potential* to reduce both duration of chest drain and hospital stay. Further studies may be required in order to fully understand and optimise the post-operative patient treatment algorithm and isolate any other factors that may influence these two parameters.

Does cessation of air leaks correspond to early chest drain removal and hospital discharge?
The early cessation of leaks following application of TissuePatch3 has not consistently lead to a reduction in the time to chest drain removal and discharge from hospital in this small patient cohort, fact which was recorded in both centres.

Several patients remained in hospital despite experiencing early postoperative chest drain removal; hence there are other factors beyond air leaks that keep patients in hospital longer.

These observations are consistent with other studies.

In summary this study supports the use of TP3 as an adjunct in the early resolution of air leaks encountered in elective lung surgery.

Therefore in centres where early discharge is solely dependent to resolution of air leaks and drain removal TP3 could influence postoperative management and reduce hospital stay with financial benefits in these units.

References

1. Rice T, Kirby T. Prolonged air leak. *Chest Surg Clin N Am*. 1992; 2:803-811
2. Stolz AJ, Schutzner J, Lischke R, Simonek J, Pafko P. Predictors of prolonged air leaks following pulmonary lobectomy. Eur J Cardiothorac Surg. 2005; 27:334-336
3. Adebonojo SA. How prolonged is “prolonged air leak”? *Ann Thorac Surg.* 1995;59:549-550
4. Tansley P, Al-Mulhim F, Ladas G, Goldstraw P. A prospective randomized controlled trial of the effectiveness of BioGlue in treating alveolar air leaks. *J Thorac Cardiovasc Surg*. 2006;132:105-112
5. Internal report on file at Tissuemed, 2008