Argentum Medical LLC

Comparative Zones of Inhibition Study

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March 2010

Several different types of commercially available silver containing wound dressings, electrolessly plated, silver vapor deposition, and silver impregnated, were analyzed via the zone of inhibition test. A non silver dressing, Johnson&Johnson Biopatch, was used as a positive control and to provide a frame of reference for antimicrobial efficacy. The Johnson&Johnson Biopatch is a foam dressing impregnated with an antibiotic (chlorhexidrine gluconate). Table 1 summarizes the type of each dressing used in the study.

Table 1. Description each silver containing wound dressing

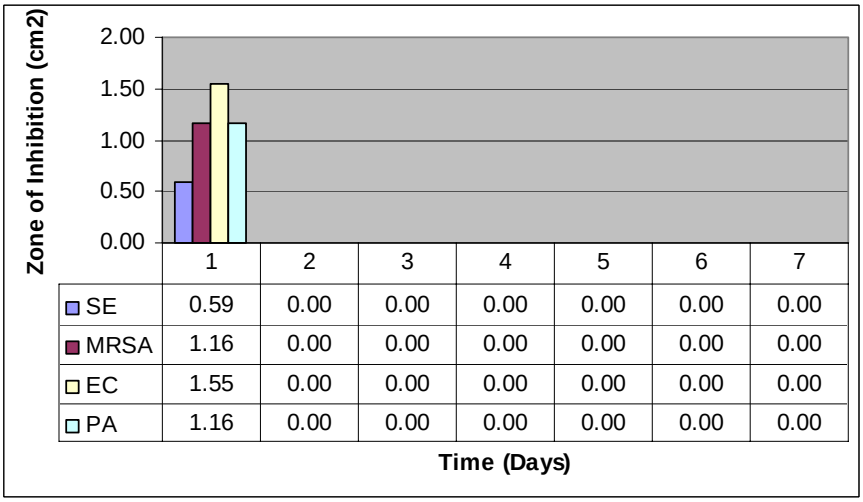
Dressing	Type
3M Tegaderm Ag Mesh	Silver Impregnated
Algidex Ag-Silver Alginate Maltodextrin	Silver Impregnated
Aquacel Ag 403765	Silver-Calcium Alginate
Aquacel Ag Rope 403712	Silver-Calcium Alginate
Coloplast Contreet	Silver Impregnated
Contreet Coloplast Hydrocolloid	Silver Impregnated
Contreet Coloplast Seasorb	Silver Impregnated
Hartman Colactive Ag 49720000	Silver Impregnated
Invacare Silver Alginate Dressing	Silver-Calcium Alginate
Johnson&Johnson Biopatch	Non-silver, Antibiotic Impregnated
Johnson&Johnson Promogran	Silver Impregnated
Johnson&Johnson Silvercel Alginate	Silver-Calcium Alginate
Medline Arglaes Powder	Powder
Medline Maxorb Alginate	Silver-Calcium Alginate
Medline Optifoam Ag	Silver Impregnated
Medline Silvasorb Cavity	Silver Impregnated
Medline Silvasorb Gel	Silver Containing Gel
Polymem Silver- Membrane	Silver Impregnated
Select Silver Antimicrobial	Silver Impregnated
Silvercel Alginate 800404	Calcium Alginate
Silverlon WCD58-NPS	Electrolessly Plated
Silverlon BCD-446	Electrolessly Plated
Silverlon Calcium Alginate CA-425	Silver-Calcium Alginate
Silverlon HT-22	Silver Impregnated
Silverlon Thick Foam SF-23	Silver Impregnated
Silverlon Wound Contact Dressing 44	Electrolessly Plated
Smith + Nephew Absorbant	Silver Impregnated
Smith+Nephew 7 Day: 20141	Vapor Deposition
Smith+Nephew Burn Dressing	Vapor Deposition

The zones of inhibition (cm^2) were calculated as the area of the bandage subtracted from the total area of the zone of clearing, as seen in Equation 1, where d is the measured diameter (cm) of the zone of inhibition.

Equation 1. $ZOI = [\pi(\frac{d}{2})^2] - [\pi(\frac{1.0}{2})^2]$

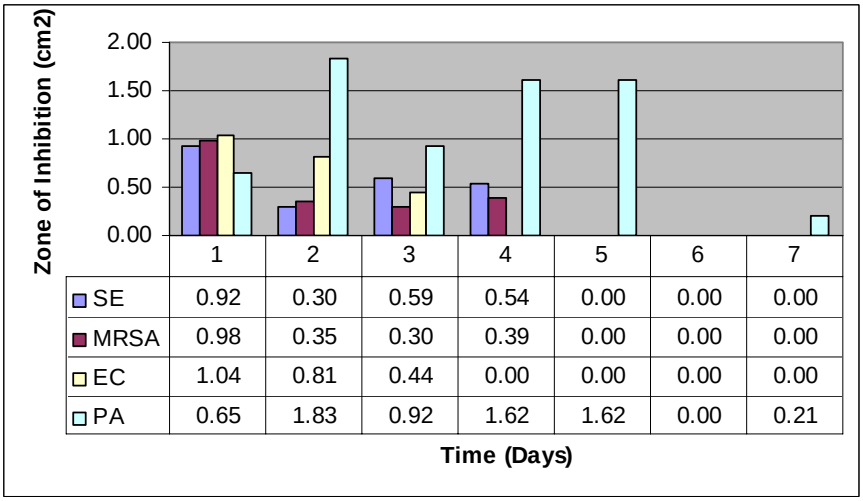
While this is not the conventional method of calculating a zone of inhibition, it is assumed to be a valid method, given that the diameters of the dressings are controlled. With this calculation, areas of bacterial inhibition are calculated. This area is a quantification of the ability of a dressing to release active silver into a medium.

There was significant variability in results of the zone of inhibition among all dressings. Figures 3-30 show the zone of inhibition trends of all the dressings tested over a seven day period. Figures 3-30 utilize the following legend: SE=*Staphylococcus* epidermis; MRSA= Methicillin Resistant *Staphylococcus* aureus; EC= *Escherichia* coli; PA=*Pseudomonas* aeruginosa



	1	2	3	4	5	6	7
SE	0.59	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	1.16	0.00	0.00	0.00	0.00	0.00	0.00
EC	1.55	0.00	0.00	0.00	0.00	0.00	0.00
PA	1.16	0.00	0.00	0.00	0.00	0.00	0.00

Figure 3. Zones of Inhibition over 7 Day Period for 3M Tegaderm Ag Mesh

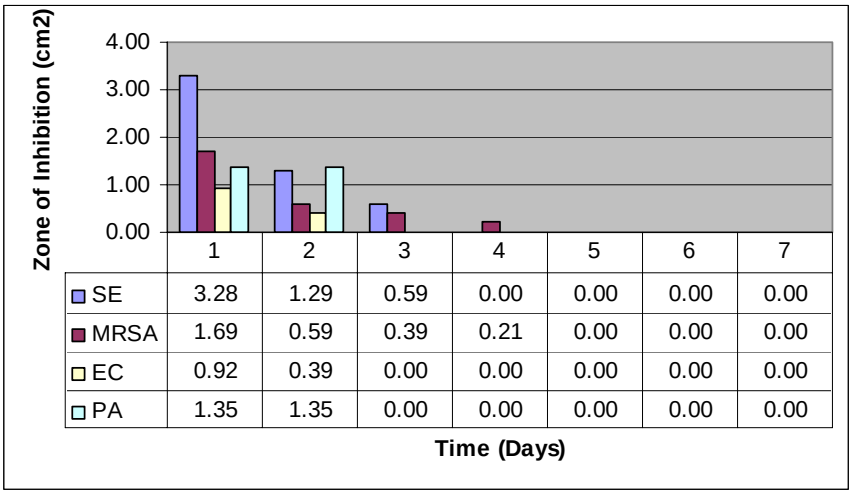


	1	2	3	4	5	6	7
SE	0.92	0.30	0.59	0.54	0.00	0.00	0.00
MRSA	0.98	0.35	0.30	0.39	0.00	0.00	0.00
EC	1.04	0.81	0.44	0.00	0.00	0.00	0.00
PA	0.65	1.83	0.92	1.62	1.62	0.00	0.21

Figure 4. Zones of Inhibition over 7 Day Period for Algidex Ag-Silver Alginate Maltodextrin

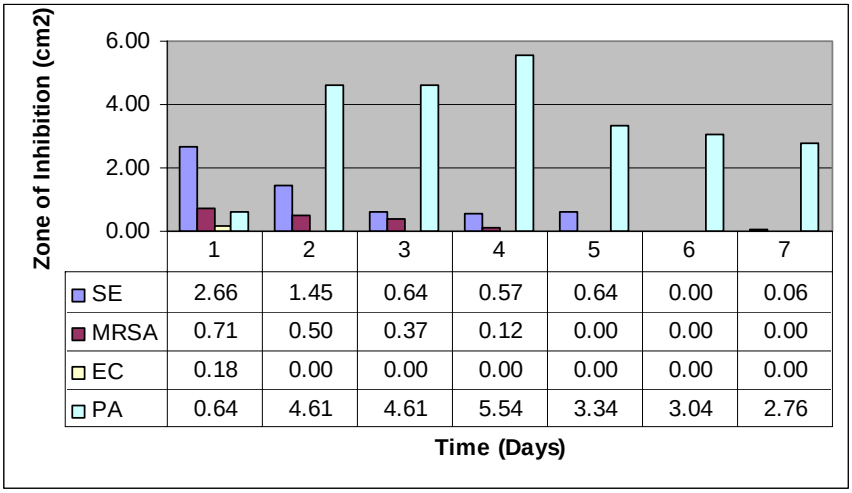
The Algidex Ag-Silver Alginate dressing showed an increased zone of inhibition for P. aeruginosa on the second day of the study. The increased zone of inhibition illustrates the usefulness of the multi day study in that this difference would be impossible to detect with a single day zone of inhibition test.

Figure 5. Zones of Inhibition over 7 Day Period for Aquacel Ag 403765



	1	2	3	4	5	6	7
SE	3.28	1.29	0.59	0.00	0.00	0.00	0.00
MRSA	1.69	0.59	0.39	0.21	0.00	0.00	0.00
EC	0.92	0.39	0.00	0.00	0.00	0.00	0.00
PA	1.35	1.35	0.00	0.00	0.00	0.00	0.00

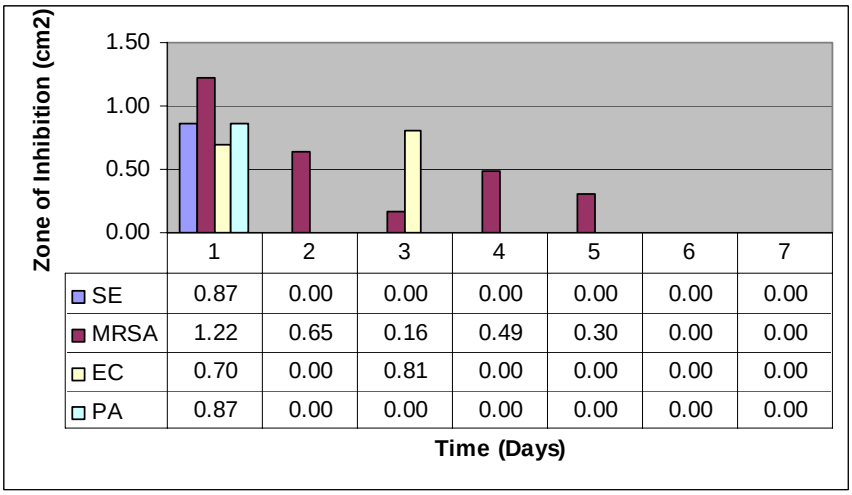
Figure 6. Zones of Inhibition over 7 Day Period for Aquacel Ag Rope 403712



	1	2	3	4	5	6	7
SE	2.66	1.45	0.64	0.57	0.64	0.00	0.06
MRSA	0.71	0.50	0.37	0.12	0.00	0.00	0.00
EC	0.18	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.64	4.61	4.61	5.54	3.34	3.04	2.76

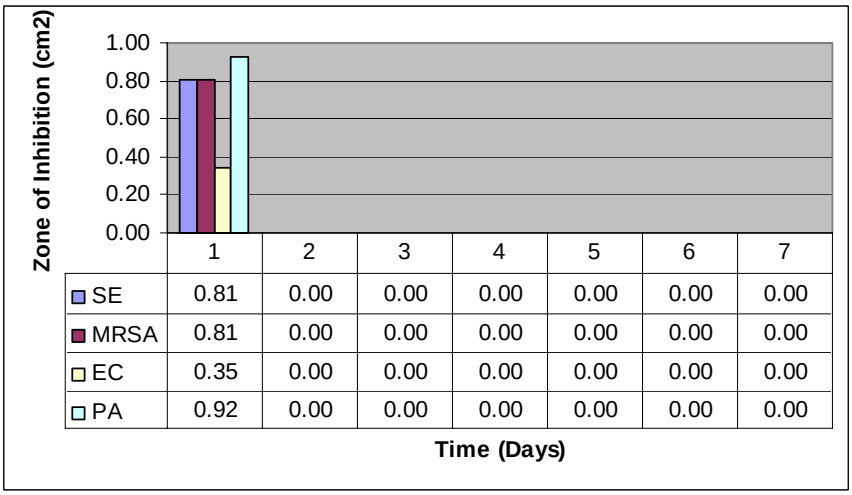
Figure 7. Zones of Inhibition over 7 Day Period for Coloplast Contreet

P. *aeruigonsa* was particuarlly susceptible to Coloplast Contreet, as the zones of inhibition stayed relatively consistent throughout the second day period with a large increase in area from day 1 to day 2.



	1	2	3	4	5	6	7
SE	0.87	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	1.22	0.65	0.16	0.49	0.30	0.00	0.00
EC	0.70	0.00	0.81	0.00	0.00	0.00	0.00
PA	0.87	0.00	0.00	0.00	0.00	0.00	0.00

Figure 8. Zones of Inhibition over 7 Day Period for Contreet Coloplast Hydrocolloid



	1	2	3	4	5	6	7
SE	0.81	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.81	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.35	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.92	0.00	0.00	0.00	0.00	0.00	0.00

Figure 9. Zones of Inhibition over 7 Day Period for Contreet Coloplast Seasorb

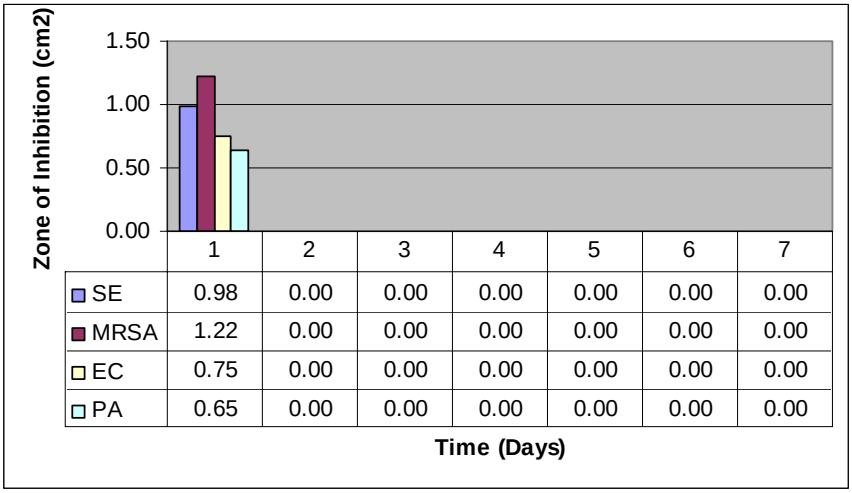


Figure 10. Zones of Inhibition over 7 Day Period for Hartman Colactive Ag 49720000

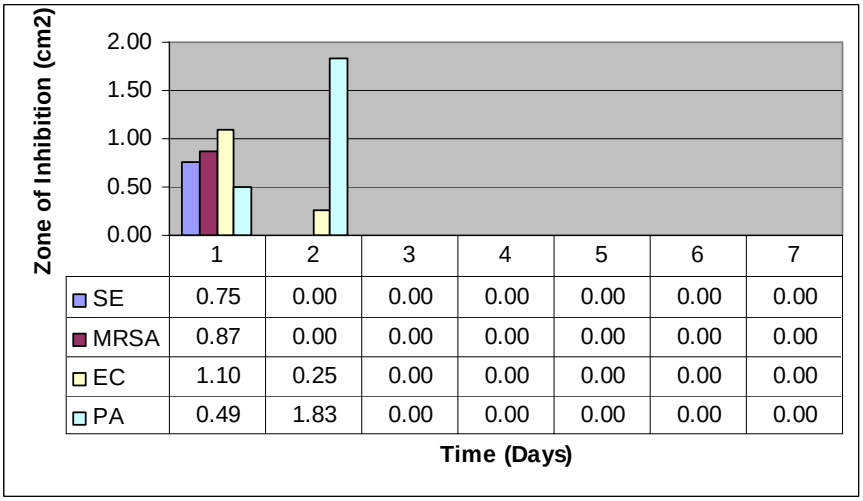
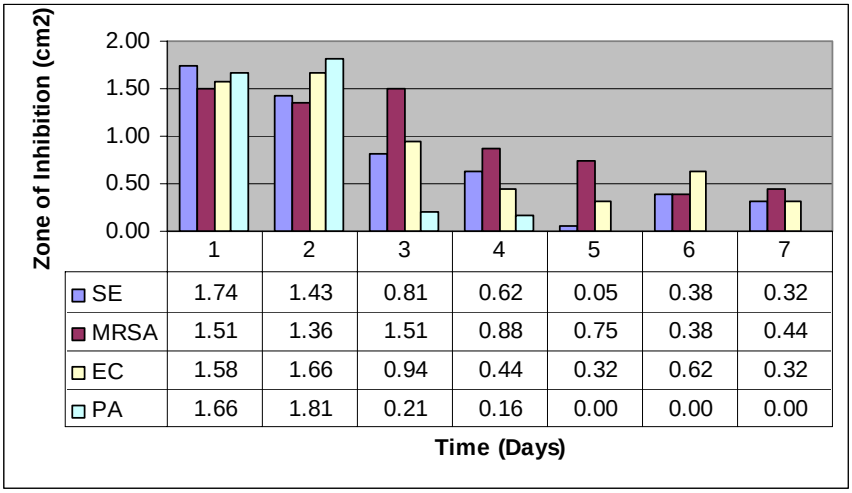


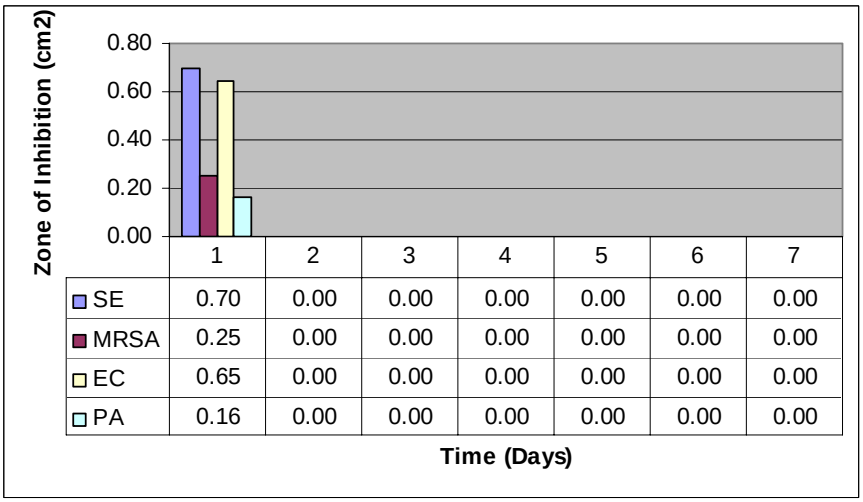
Figure 11. Zones of Inhibition over 7 Day Period for Invacare Silver Alginate Dressing



	1	2	3	4	5	6	7
SE	1.74	1.43	0.81	0.62	0.05	0.38	0.32
MRSA	1.51	1.36	1.51	0.88	0.75	0.38	0.44
EC	1.58	1.66	0.94	0.44	0.32	0.62	0.32
PA	1.66	1.81	0.21	0.16	0.00	0.00	0.00

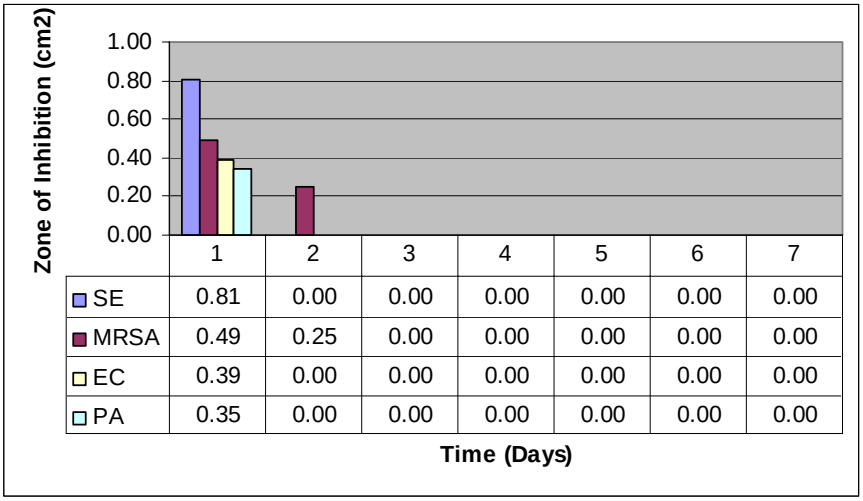
Figure 12. Zones of Inhibition over 7 Day Period for Johnson and Johnson Biopatch

Note that the Johnson&Johnson Biopatch is the antibiotic impregnated control dressing.



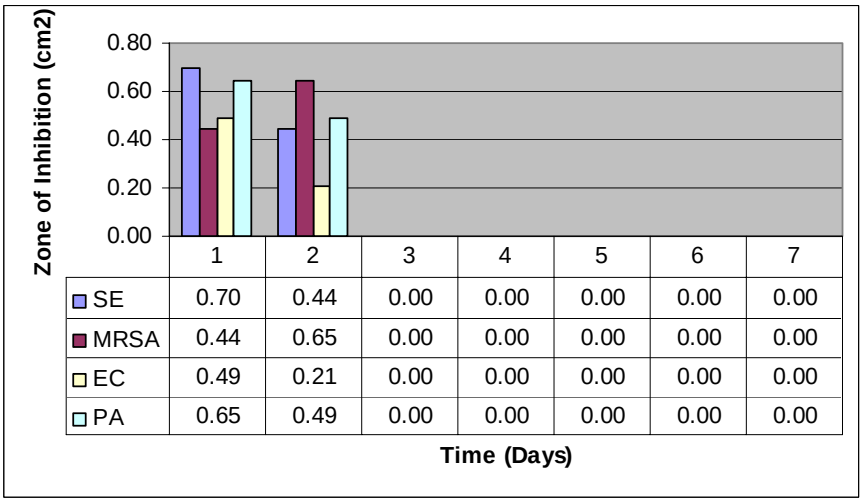
	1	2	3	4	5	6	7
SE	0.70	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.25	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.65	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.16	0.00	0.00	0.00	0.00	0.00	0.00

Figure 13. Zones of Inhibition over 7 Day Period for Johnson and Johnson Promogran



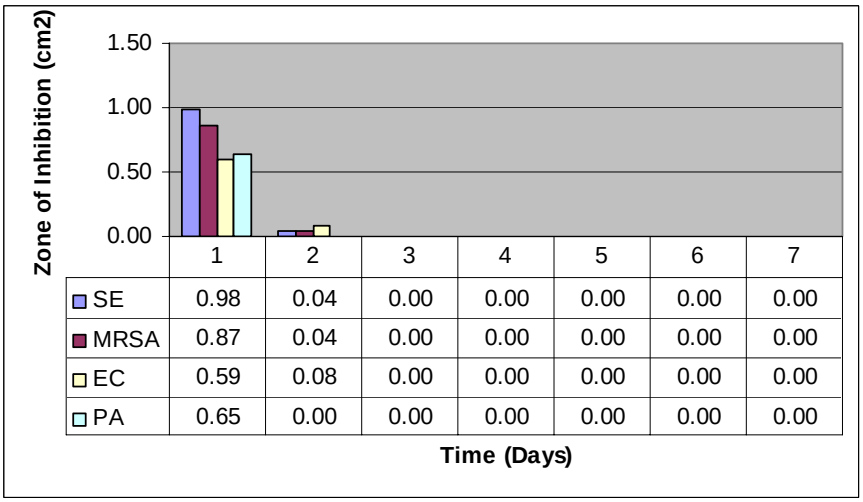
	1	2	3	4	5	6	7
SE	0.81	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.49	0.25	0.00	0.00	0.00	0.00	0.00
EC	0.39	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.35	0.00	0.00	0.00	0.00	0.00	0.00

Figure 14. Zones of Inhibition over 7 Day Period for Johnson and Johnson Silvercel Alginate



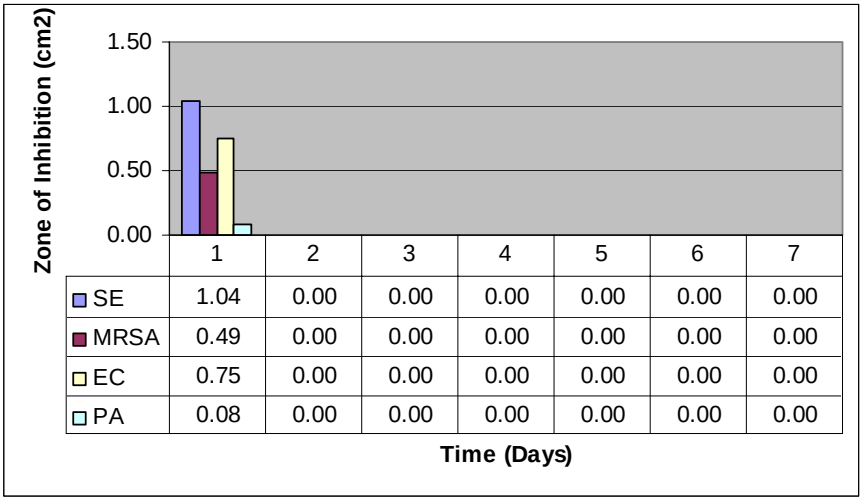
	1	2	3	4	5	6	7
SE	0.70	0.44	0.00	0.00	0.00	0.00	0.00
MRSA	0.44	0.65	0.00	0.00	0.00	0.00	0.00
EC	0.49	0.21	0.00	0.00	0.00	0.00	0.00
PA	0.65	0.49	0.00	0.00	0.00	0.00	0.00

Figure 15. Zones of Inhibition over 7 Day Period for Medline Arglaes Powder



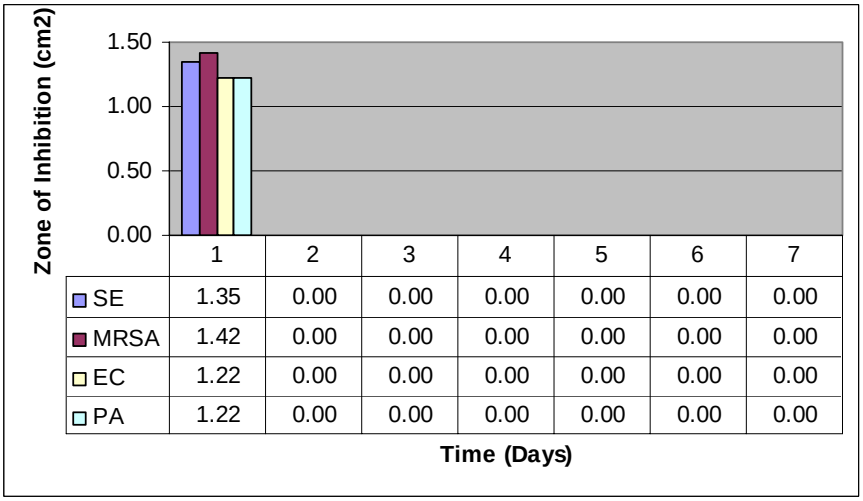
	1	2	3	4	5	6	7
SE	0.98	0.04	0.00	0.00	0.00	0.00	0.00
MRSA	0.87	0.04	0.00	0.00	0.00	0.00	0.00
EC	0.59	0.08	0.00	0.00	0.00	0.00	0.00
PA	0.65	0.00	0.00	0.00	0.00	0.00	0.00

Figure 16. Zones of Inhibition over 7 Day Period for Medline Maxorb Alginate



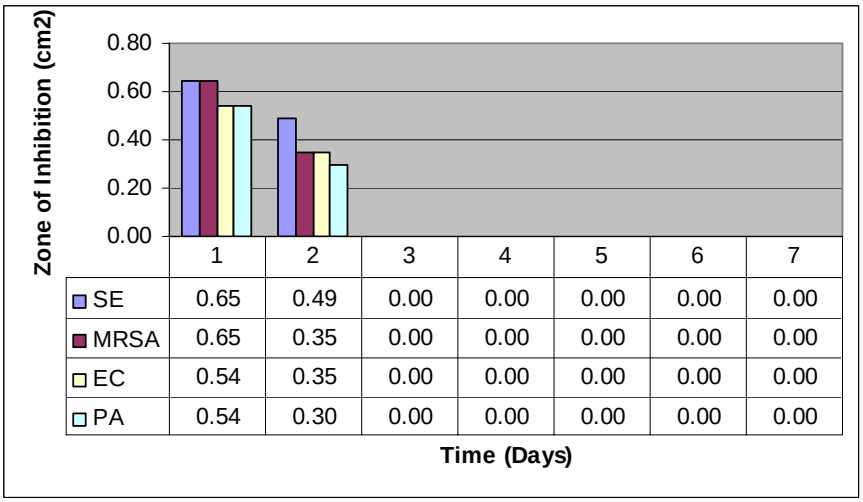
	1	2	3	4	5	6	7
SE	1.04	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.49	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.75	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.08	0.00	0.00	0.00	0.00	0.00	0.00

Figure 17. Zones of Inhibition over 7 Day Period for Medline Optifoam Ag



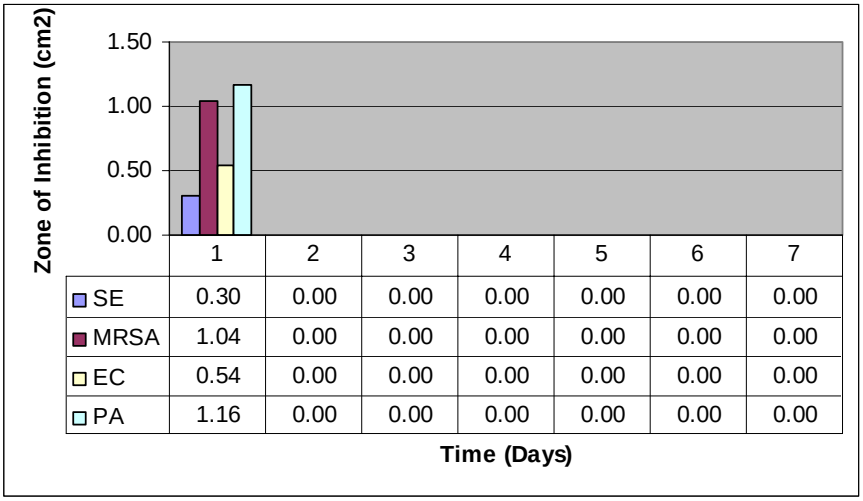
	1	2	3	4	5	6	7
SE	1.35	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	1.42	0.00	0.00	0.00	0.00	0.00	0.00
EC	1.22	0.00	0.00	0.00	0.00	0.00	0.00
PA	1.22	0.00	0.00	0.00	0.00	0.00	0.00

Figure 18. Zones of Inhibition over 7 Day Period for Medline Silvasorb Cavity



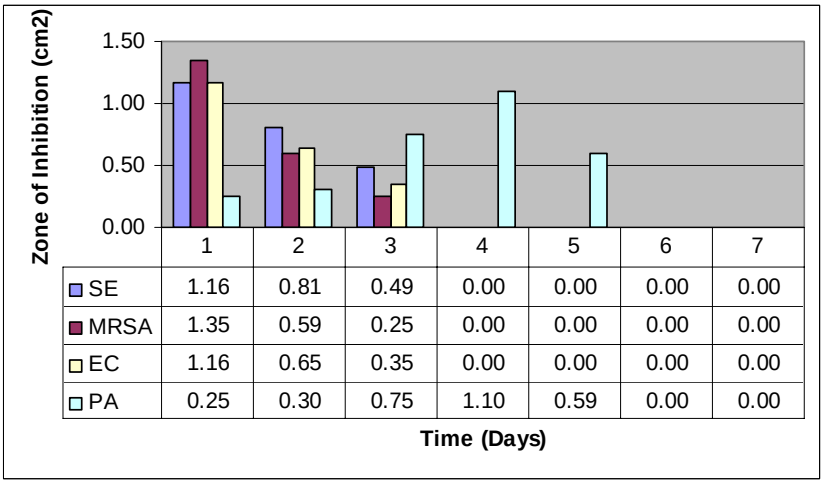
	1	2	3	4	5	6	7
SE	0.65	0.49	0.00	0.00	0.00	0.00	0.00
MRSA	0.65	0.35	0.00	0.00	0.00	0.00	0.00
EC	0.54	0.35	0.00	0.00	0.00	0.00	0.00
PA	0.54	0.30	0.00	0.00	0.00	0.00	0.00

Figure 19. Zones of Inhibition over 7 Day Period for Medline Silvasorb Gel



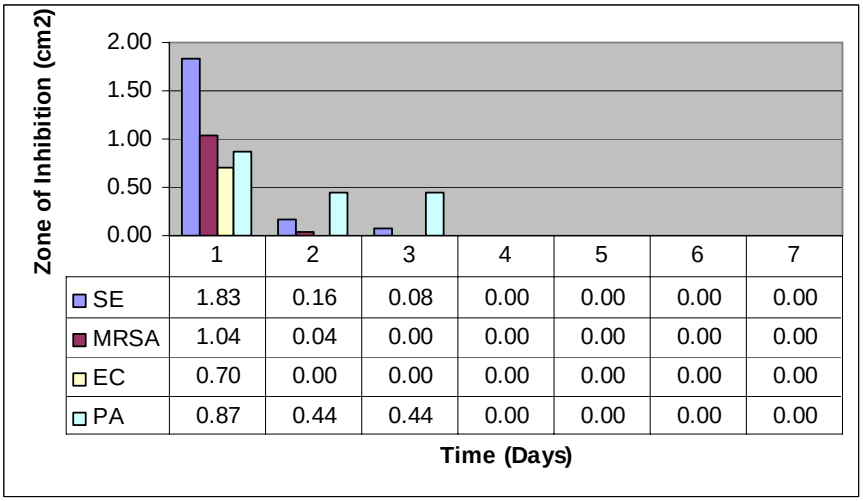
	1	2	3	4	5	6	7
SE	0.30	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	1.04	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.54	0.00	0.00	0.00	0.00	0.00	0.00
PA	1.16	0.00	0.00	0.00	0.00	0.00	0.00

Figure 20. Zones of Inhibition over 7 Day Period for Polymem Silver-Membrane



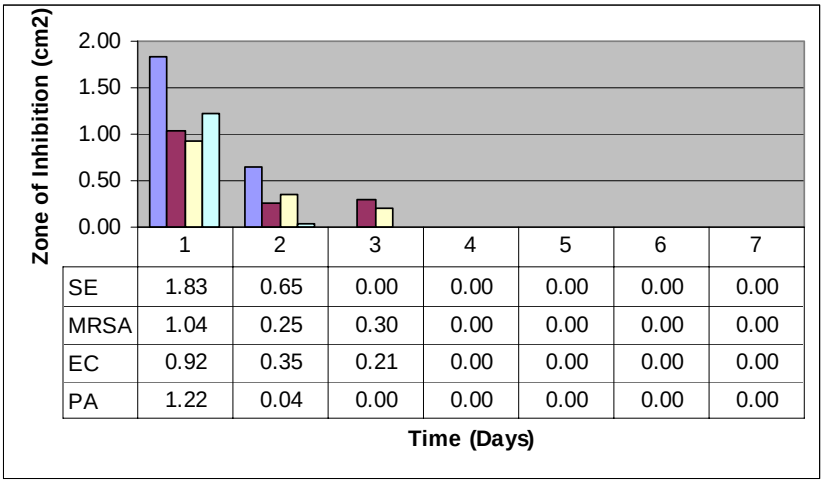
	1	2	3	4	5	6	7
SE	1.16	0.81	0.49	0.00	0.00	0.00	0.00
MRSA	1.35	0.59	0.25	0.00	0.00	0.00	0.00
EC	1.16	0.65	0.35	0.00	0.00	0.00	0.00
PA	0.25	0.30	0.75	1.10	0.59	0.00	0.00

Figure 21. Zones of Inhibition over 7 Day Period for Select Silver Antimicrobial



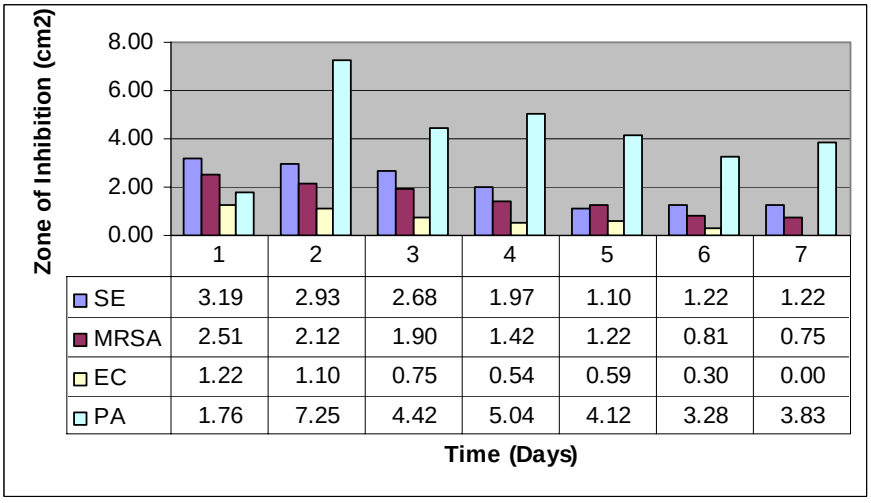
	1	2	3	4	5	6	7
SE	1.83	0.16	0.08	0.00	0.00	0.00	0.00
MRSA	1.04	0.04	0.00	0.00	0.00	0.00	0.00
EC	0.70	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.87	0.44	0.44	0.00	0.00	0.00	0.00

Figure 22. Zones of Inhibition over 7 Day Period for Silvercel Alginate 800404



	1	2	3	4	5	6	7
SE	1.83	0.65	0.00	0.00	0.00	0.00	0.00
MRSA	1.04	0.25	0.30	0.00	0.00	0.00	0.00
EC	0.92	0.35	0.21	0.00	0.00	0.00	0.00
PA	1.22	0.04	0.00	0.00	0.00	0.00	0.00

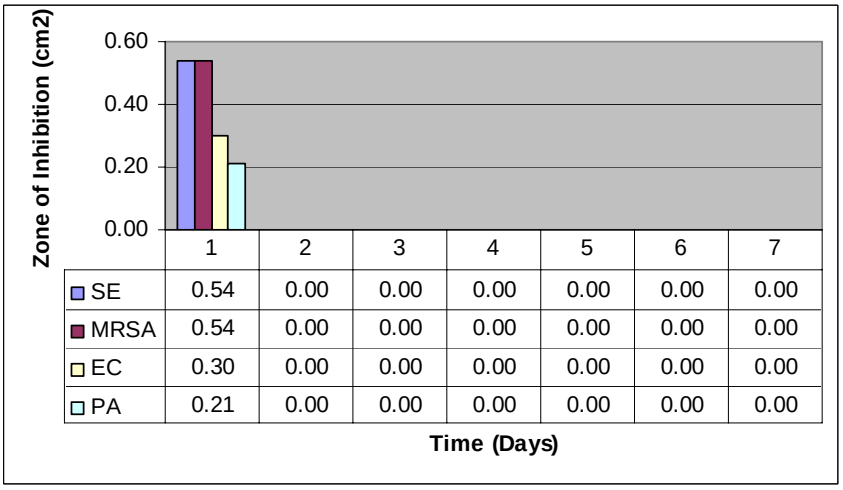
Figure 23. Zones of Inhibition over 7 Day Period for Silverlon WCD58-NPS



	1	2	3	4	5	6	7
SE	3.19	2.93	2.68	1.97	1.10	1.22	1.22
MRSA	2.51	2.12	1.90	1.42	1.22	0.81	0.75
EC	1.22	1.10	0.75	0.54	0.59	0.30	0.00
PA	1.76	7.25	4.42	5.04	4.12	3.28	3.83

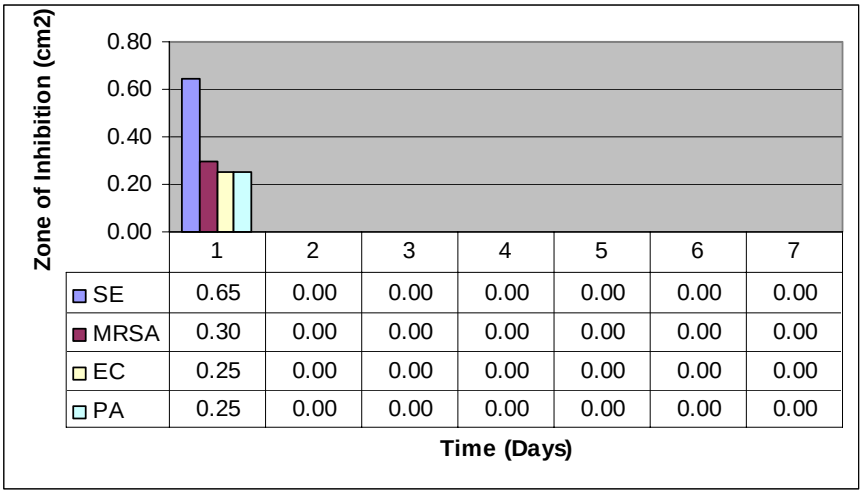
Figure 24. Zones of Inhibition over 7 Day Period for Silverlon Burn Contact Dressing-446

The Silverlon Burn Contact Dressing showed the largest zones of inhibition over the full seven Day time frame.



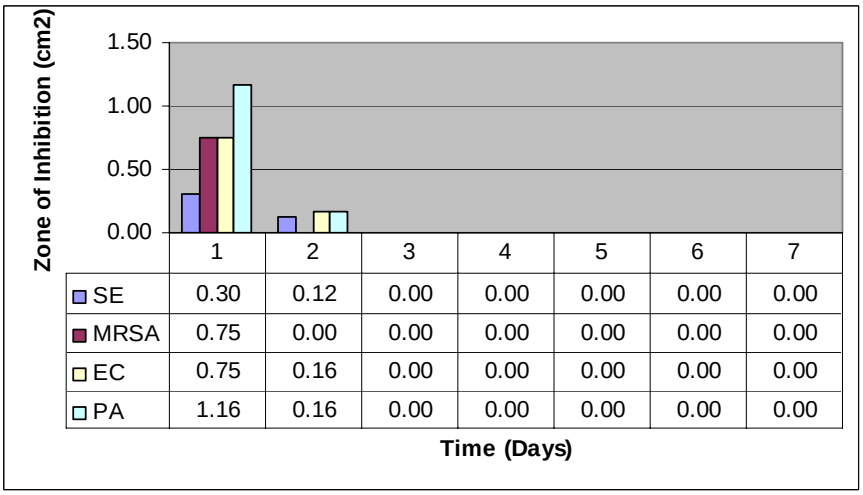
	1	2	3	4	5	6	7
SE	0.54	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.54	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.30	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.21	0.00	0.00	0.00	0.00	0.00	0.00

Figure 25. Zones of Inhibition over 7 Day Period for Silverlon Calcium Alginate CA-425



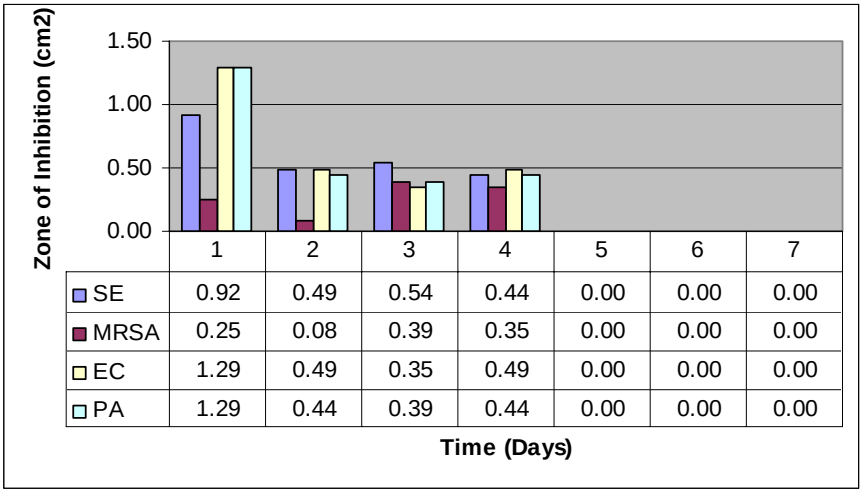
	1	2	3	4	5	6	7
SE	0.65	0.00	0.00	0.00	0.00	0.00	0.00
MRSA	0.30	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.25	0.00	0.00	0.00	0.00	0.00	0.00
PA	0.25	0.00	0.00	0.00	0.00	0.00	0.00

Figure 26. Zones of Inhibition over 7 Day Period for Silverlon Thick Foam SF-23



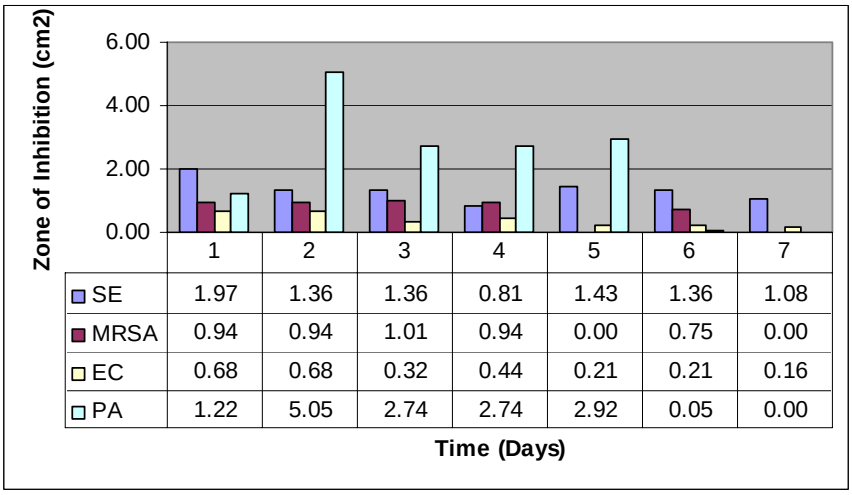
	1	2	3	4	5	6	7
SE	0.30	0.12	0.00	0.00	0.00	0.00	0.00
MRSA	0.75	0.00	0.00	0.00	0.00	0.00	0.00
EC	0.75	0.16	0.00	0.00	0.00	0.00	0.00
PA	1.16	0.16	0.00	0.00	0.00	0.00	0.00

Figure 27. Zones of Inhibition over 7 Day Period for Silverlon Wound Contact Dressing 44



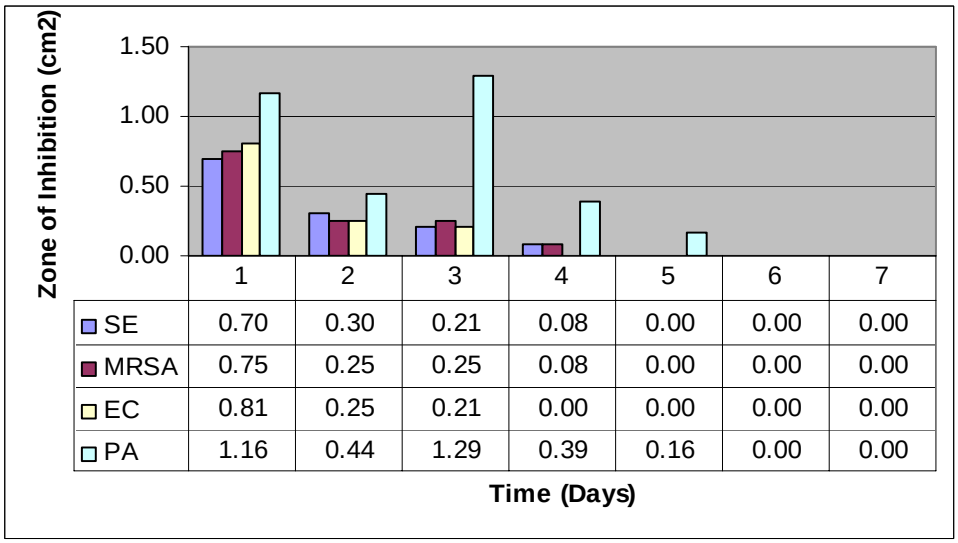
	1	2	3	4	5	6	7
SE	0.92	0.49	0.54	0.44	0.00	0.00	0.00
MRSA	0.25	0.08	0.39	0.35	0.00	0.00	0.00
EC	1.29	0.49	0.35	0.49	0.00	0.00	0.00
PA	1.29	0.44	0.39	0.44	0.00	0.00	0.00

Figure 28. Zones of Inhibition over 7 Day Period for Smith+Nephew Absorbant



	1	2	3	4	5	6	7
SE	1.97	1.36	1.36	0.81	1.43	1.36	1.08
MRSA	0.94	0.94	1.01	0.94	0.00	0.75	0.00
EC	0.68	0.68	0.32	0.44	0.21	0.21	0.16
PA	1.22	5.05	2.74	2.74	2.92	0.05	0.00

Figure 29. Zones of Inhibition over 7 Day Period for Smith+Nephew 7 Day 20141
The Smith+Nephew 7 Day dressing produced relatively large zones over the full 7 day period.



	1	2	3	4	5	6	7
SE	0.70	0.30	0.21	0.08	0.00	0.00	0.00
MRSA	0.75	0.25	0.25	0.08	0.00	0.00	0.00
EC	0.81	0.25	0.21	0.00	0.00	0.00	0.00
PA	1.16	0.44	1.29	0.39	0.16	0.00	0.00

Figure 30. Zones of Inhibition over 7 Day Period for Smith+Nephew Burn Dressing

The Silverlon Hydrocolloid did not produce measurable zones of inhibition for any bacteria.

Clearly, the performance on the zone of inhibition test varied considerably. Ideally, a dressing would release sufficient silver to produce measurable zones of inhibition over the full seven day period. Presumably, this would translate to a dressing that releases significant amounts of silver into a wound over a multi day period. Such a dressing would exert antimicrobial effects while not needing to be changed very frequently, thus reducing complications of the wound bed in both instances. Therefore, the number of days zones of inhibition were noted as well as the measured zones of inhibition should be considered when evaluating the efficacy of the dressings. The 2 and 7 day medians provide a comparison of antimicrobial efficacy.

In order to rank the dressings in terms of antimicrobial efficacy, zones of inhibition were considered for all bacterial challenges over a 2 and 7 day period. A Kurskal-Wallis one way analysis of variance on ranks was performed on the zones of inhibition for all bacterial challenges to rank each dressing and Dunn's Method was utilized to determine which dressings produced zones of inhibition comparable to the Johnson & Johnson Biopatch over a 2 and 7 day period. Dressings were ranked first according to their median, then according to mean if a tie resulted. Dressings that produced zones of inhibition statistically similar to the Johnson & Johnson Biopatch were categorized as "high" antimicrobial efficacy, whereas those dressings that produced zones statistically smaller than the Johnson & Johnson Biopatch were categorized as "low" antimicrobial efficacy. Table 2 summarizes the ranks and categories of the 2 day study, whereas Table 3 summarizes the ranks and categories of the 7 day study.

Table 2. Summary of mean and median zones of inhibition for all bacterial challenges and categories of antimicrobial efficacy for dressings during a 2 day period

Dressing	2 Day Mean Zone of Inhibition (cm^2)	2 Day Median Zone of Inhibition (cm^2)	2 Day Antimicrobial Efficacy
Silverlon BCD-445	2.76	2.05	High
Johnson&Johnson Biopatch	1.59	*1.51*	*High*
Aquacel Ag 403765	1.23	1.29	High
Aquacel Ag Rope 403712	1.36	1.23	High
Smith+Nephew 7 Day: 20141	1.61	1.15	High
Algidex Ag-Silver Alginate Maltodextrin	0.86	0.87	High
Silverlon WCD58-NPS	0.79	0.81	High
Coloplast Contreet	1.34	0.78	High
Select Silver Antimicrobial	0.78	0.7	High
Contreet Coloplast Hydrocolloid	0.54	0.7	Low
Invacare Silver Alginate Dressing	0.66	0.59	Low
Silvercel Alginate 800404	0.64	0.54	Low
Smith+Nephew Burn Dressing	0.58	0.54	Low
Smith + Nephew Absorbant	0.66	0.49	Low
Medline Arglaes Powder	0.51	0.49	Low
Medline Silvasorb Gel	0.48	0.49	Low

Johnson&Johnson Silvercel Alginate	0.29	0.35	Low
Medline Maxorb Alginate	0.41	0.31	Low
Hartman Colactive Ag 49720000	0.45	0.27	Low
3M Tegaderm Ag Mesh	0.56	0.27	Low
Silverlon Wound Contact Dressing 44	0.43	0.21	Low
Contreet Coloplast Seasorb	0.36	0.17	Low
Silverlon Calcium Alginate CA-425	0.20	0.08	Low
Silverlon Thick Foam SF-23	0.18	0.08	Low
Johnson&Johnson Promogran	0.22	0.04	Low
Medline Silvasorb Cavity	0.65	0	Low
Polymem Silver- Membrane	0.38	0	Low
Medline Optifoam Ag	0.30	0	Low
Silverlon HT-22	0.00	0	Low

As seen in Table 2, 8 dressings produced zones of inhibition statistically similar to the Johnson & Johnson Biopatch over a 2 day period and therefore were considered antimicrobial efficacious. The rest of the dressings (20) produced zones of inhibition statistically smaller than the Johnson & Johnson Biopatch, and were therefore considered ineffective ($p<0.05$). The dressings were ranked first according to median, then mean zones of inhibition if a tie resulted.

Table 3. Summary of mean and median zones of inhibition for all bacterial challenges and categories of antimicrobial efficacy for dressings during a 7 day period

Dressing	7 Day Mean Zone of Inhibition (cm^2)	7 Day Median Zone of Inhibition (cm^2)	7 Day Antimicrobial Efficacy
Silverlon BCD-445	2.12	1.48	High
Smith+Nephew 7 Day: 20141	1.12	0.88	High
Johnson&Johnson Biopatch (control)	*0.78*	*0.68*	*High*
Coloplast Contreet	1.16	0.37	Low*
Algidex Ag-Silver Alginate Maltodextrin	0.48	0.35	Low*
Smith + Nephew Absorbant	0.31	0.21	Low
Select Silver Antimicrobial	0.35	0.13	Low
Smith+Nephew Burn Dressing	0.26	0.08	Low
Aquacel Ag Rope 403712	0.43	0	Low
Aquacel Ag 403765	0.40	0	Low
Silverlon WCD58-NPS	0.24	0	Low
Contreet Coloplast Hydrocolloid	0.22	0	Low
Silvercel Alginate 800404	0.20	0	Low
Invacare Silver Alginate Dressing	0.19	0	Low
Medline Silvasorb Cavity	0.19	0	Low
3M Tegaderm Ag Mesh	0.16	0	Low
Medline Arglaes Powder	0.15	0	Low
Medline Silvasorb Gel	0.14	0	Low
Hartman Colactive Ag 49720000	0.13	0	Low
Silverlon Wound Contact Dressing 44	0.12	0	Low
Medline Maxorb Alginate	0.12	0	Low
Polymem Silver- Membrane	0.11	0	Low
Contreet Coloplast Seasorb	0.10	0	Low

Medline Optifoam Ag	0.08	0	Low
Johnson&Johnson Silvercel Alginate	0.08	0	Low
Johnson&Johnson Promogran	0.06	0	Low
Silverlon Calcium Alginate CA-425	0.06	0	Low
Silverlon Thick Foam SF-23	0.05	0	Low
Silverlon HT-22	0.00	0	Low

*Although the median zone of inhibition over the 7 day study was statistically similar to the Johnson&Johnson Biopatch, these dressings did not produce measurable zones of inhibition for all bacteria over the full seven day time frame.

As seen in Table 3, 4 dressings produced zones of inhibition statistically similar to the Johnson & Johnson Biopatch over a 7 day period and therefore were considered antimicrobial efficacious. The rest of the dressings (24) produced zones of inhibition statistically smaller than the Johnson & Johnson Biopatch, and were therefore considered ineffective ($p<0.05$). The dressings were ranked first according to their median zones then mean zones of inhibition if a tie resulted.

The majority of dressings were ineffective for a 7 day period. Only 2 dressings, the Silverlon Burn Contact Dressing, or the Smith+Nephew 7 Day Dressing, produced measurable zones of inhibition for 7 days and zones of inhibition statistically similar to the Johnson & Johnson Biopatch. Contreet Coloplast and Algidex Silver Alginate with Maltodextrin produced median zones of inhibition statistically similar to the positive control, but they did not maintain measurable zones of inhibition for the full 7 day time frame. There was not a statistically significant difference between the control,. There was a statistically significant difference between the Silverlon Burn Contact Dressing and both Contreet Coloplast and Algidex ($p<0.05$, $p<0.05$).