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MECHANICAL PROPERTIES OF HTR(R)

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Danette Skowronski Taylor

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MECHANICAL PROPERTIES OF HTR®

BY

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ABSTRACT

MECHANICAL PROPERTIES OF HTR®

BY

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Attention has been focused on the need for substitutes for natural bone graft. This research examined the compressive mechanics of and implant potential of one such substitute: Hard Tissue Replacement, or HTR®.

HTR® was molded by the manufacturer into dowels representative of the shape used in the Cloward anterior spinal fusion. The dowels were tested along axial and diametric compression. The load-deformation curves generated were analyzed to obtain stiffness, yield load and peak load. The data from the diametric tests was compared to the results of similar tests run on natural bone dowels.

A study to explore the amount of bony ingrowth into HTR® was run in conjunction with the mechanical testing. Plugs were implanted in canine cervical spines; after a designated time, the implants were examined histologically for evidence of ingrowth.

HTR® had yield loads from 74 - 216% higher than natural bone. Stiffness averaged 31% higher. Results of the implantation study showed clear signs of bony ingrowth without gross evidence of inflammation.

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INTRODUCTION

Foreign materials have been used as implants to strengthen bony material since the sixteenth century (10). Over the years, substances ranging from metal to plastic and coral to natural bone have been employed in an attempt to increase the strength and therefore the function of various bones within the body.

Of this variety of materials, natural bone has long been considered the "ideal" graft substance for use in bony structures: natural bone is hydrophilic, osteogenic, and strong. Additionally, there are three potential sources of natural bone which can be harvested for use as graft: xenograft, bone from a species separate from that which the graft will be used in; allograft, bone from a different individual of the same species as the recipient; and autograft, bone taken from one location for use in a separate location within the same individual (15).

Problems are inherent within each of these types of grafts. The use of autologous bone requires a second major surgical procedure to obtain the graft, which can contribute to an increase in morbidity. Xenograft and allograft carry a risk of inducing an immunogenic response as well as the danger of infection. Although sterilization protocols are required, the procedures commonly used -- lyophiliztion and/or gamma irradiation -- have been shown to damage the structural integrity of the graft (38).

The need for an artificial grafting material, allowing circumvention of the problems outlined above, is apparent. However, a successful graft must meet all the criteria on a formidable list. The ideal bone substitute has been described as being biologically inert, readily available, easily adaptable to the site in which it is implanted, and ultimately, replaceable by host tissue, that is, biodegradable (4, 5, 35). It can be argued that the biodegradation of a material is not necessary, provided the other criteria are satisfied and the tissue surrounding the graft is able to adapt as required by environmental changes (5).

Presented here are the preliminary results of research on a synthetic graft material trade-named Hard Tissue Replacement, or HTR®, with comparison made to the compressive strength of trabecular bone (Figure 1). This material is a polymeric composite constructed of poly methylmethacrylate (PMMA) and poly hydroxyethyl methacrylate (PHEMA). In a patented process, a core of PMMA is coated with an envelope of PHEMA; the result is a granular or beaded substance, each bead maintaining a hydrophobic (PMMA) interior and a hydrophilic (PHEMA) exterior. This material can be left in a loose granular form or heat-molded into various shapes. FDA approval for HTR® use in dental applications such as alveolar ridge augmentation or as a filling within bony defects has already been obtained (3, 4). Reports from case studies

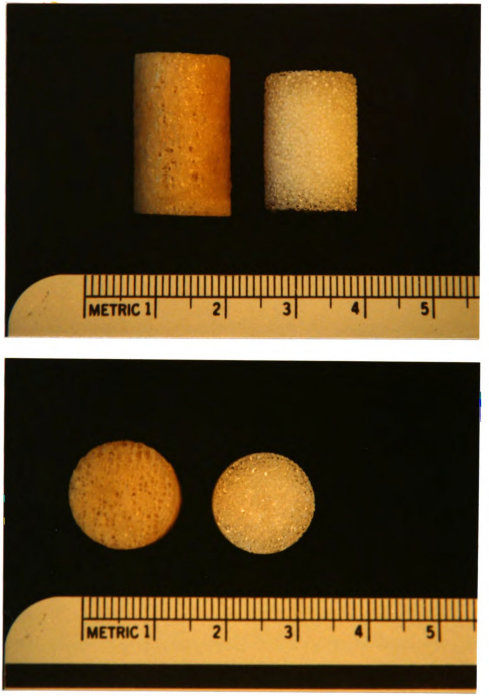


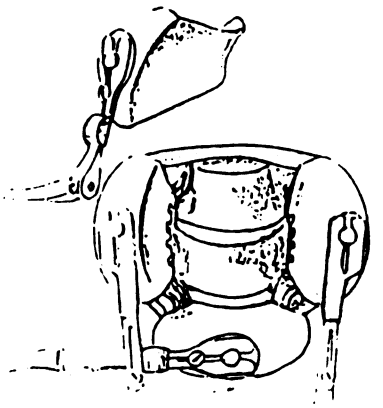
FIGURE 1: Photograph showing structural comparison of trabecular bone (left) and HTR®.

indicate that HTR® is a light-weight scaffold which bone easily surrounds and penetrates (3). This suggests that HTR® may easily adapt to other bony areas where graft is needed.

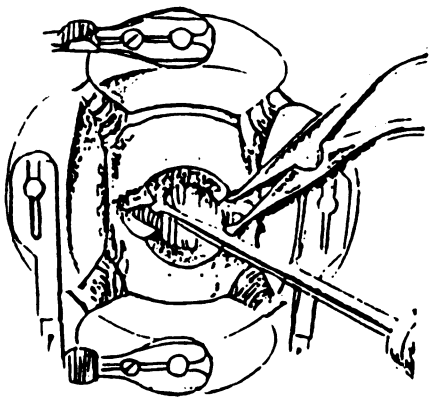
This research program used a Cloward plug model, which was one of the first widely accepted uses of graft material in the U.S. The procedure replaces a defective disc within the cervical spine with a cylindrical dowel of bone, thereby maintaining disc space and protecting the nerve roots which exit the spinal cord in the area (14) (Figure 2).

The graft used must maintain structural function until fusion of the vertebral bodies surrounding the graft is complete -- occasionally as long as six months (41). If the graft fails during fusion, nerve root impingement and subsequent tissue damage following collapse of the graft is a possibility.

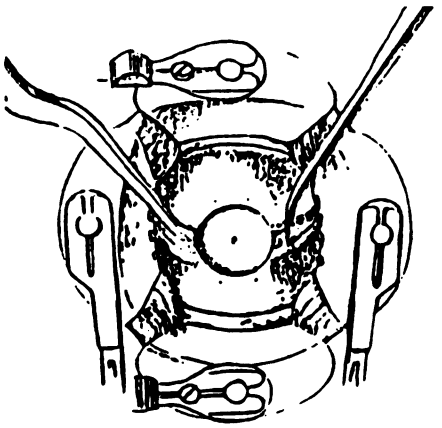
While it is recognized that additional forces such as torsion and bending also act upon the graft (23), the initial load that the graft must bear is compression; therefore, this study was solely a comparison of direct compressive loads on HTR® and trabecular bone. A variety of environments were tested in an attempt to simulate physiologic or in-vivo surroundings.



Exposed vertebral column (anterior view)



Vertebral disc removed; space for Cloward dowel enlarged



Allograft dowel in place within vertebral column

FIGURE 2: Simplified Cloward procedure.

LITERATURE SURVEY

From the year 1775, when in France a metal wire was used to fasten together fragments of a shattered humerus (42), there have been attempts to improve the healing process of the human body by the implantation of foreign substances. However, it was not until aseptic surgical technique was developed by Lister (32) almost a full century later that implants were successful in helping to repair defects within the human structure.

With the development of sterile technique came the first successful transplant of bone between individuals in 1878 (27). Ten years later, Fraenkel (19) successfully implanted a plastic material when he used celluloid to fill large defects in canine skulls.

The onset of the twentieth century brought increased knowledge about natural bone grafts. This data included information regarding antigenicity, graft strength, and controversy over how the grafts were ultimately incorporated into the body. Nonetheless, it was not until 1950 that a formalized method for collecting and preserving bone and other tissues for transplant purposes was developed by the U.S. Navy (11).

As the number of tissues available for transplantation increased, so too did the rate of infection following implantation. In 1955 Carr and Hyatt (13) hypothesized that greater than ten percent of transplanted

grafts at that time acted to introduce infection into the recipient. This high rate of infection occurred in spite of the careful tissue banking procedure developed by the Navy, which eliminated graft procurement from a donor if the cause of death had contaminated the tissues in any way (11).

In an effort to combat this rate of infection, Carr, et al (13) proposed freeze-drying or lyophilization as a method of sterilizing the tissue grafts. While this treatment prolonged the storage time of the tissue, it was not effective in reducing the rate of infection. In 1958 DeVries, et al (16) suggested the use of radioactive cobalt (cobalt 60) as a means to sterilize contaminated bone.

With increased handling and processing, the integrity of bone grafts decreased. Triantafyllou, et al (38) showed that with combined freeze-drying and sterilization with gamma irradiation the strength of bone was decreased in most cases to less than 30 percent of comparable fresh bone specimens. Using these results and the results of independent tests which confirmed Triantafyllou's findings, Pelker, et al (33) developed a hypothesis which cautioned that the methods of sterilization and storage of a graft be carefully examined prior to its implantation to avoid the possibility of placing the bone into a location where failure was inevitable.

As research on natural bone developed, research on plastics as implant materials was continuing. In 1945, Blaine (8) successfully implanted a sterile dough of methyl methacrylate into gaps in the skulls of cats and rabbits. No pathological tissue reaction occurred and three months after the implantation ossified tissue was seen in the space between the meninges and the implanted plastic.

Hamby, et al (20) attempted to compete in the field of neurosurgery when, in 1959, he replaced ruptured lumbar vertebral discs with methyl methacrylate. Hamby's patients all recovered successfully. However, no significant difference was found in either length of hospital stay or post-operative function when his subjects were compared to a group of patients with ruptured discs who underwent traditional treatment of discectomy only.

No further notable developments occurred until the mid-1970's. While attempting to develop a material suitable for tooth replacement, Taylor and Smith (36) determined that porous methyl methacrylate was a suitable implant in fibrous tissue with a notable lack of tissue reaction. They did stipulate that the pore size of the material was to be controlled so that vascular penetration of the graft could occur.

In 1977, Ashman, et al (5) also determined that porous poly methlymethacrylate was suitable for tissue implantation. Paralleling Taylor's results, Ashman stated that the pore size within the implant material appeared to

have an effect on the optimal location of that implant. Ashman's research stated that a one-hundred micron (100 um) pore size was adequate for connective tissue ingrowth in an osseous site and a 450 micron (um) size was necessary for bony ingrowth in the same site.

During this same time period, Ashman, et al (2) successfully implanted methyl methacrylate into canine alveolar ridge spaces following extraction of natural teeth. In each case, a methyl methacrylate replica of each tooth removed was implanted immediately into the socket of each natural tooth. After six months, there was no evidence of alveolar ridge resorption; in addition, normal osteoblastic and osteoclastic activity was seen at the junction of the alveolar bone and the implants.

Approximately 10 years later, Duff (18) found that the use of methyl methacrylate in conjunction with bone screws over a field of not more than three vertebral bodies was a safe and effective method of providing both immediate and long-term stabilization for traumatic cervical spine fracture-dislocation.

With advancing technology, new materials continue to be introduced as possible substitutes for bone. Coralline hydroxyapatite, ceramics (calcium hydroxyapatite and tricalcium phosphate) and new polymeric substances (Hard Tissue Replacement or HTR®) have been tested as implants with encouraging results. In each case, when these materials are implanted, bone has been seen growing

within the pores of the implant with little or no pathological tissue response elicited (3, 4, 7, 22, 23, 35, 37, 39).

As more organisms become resistant to present day pharmacopaeia and new, often lethal, diseases continue to evolve it is conceivable that the current practice of transplanting tissue from one individual to another will be slowly abolished. As this occurs, it is imperative that adequate substitutes be developed. This paper looks at the mechanical properties of one such substitute, HTR®, and compares these properties with the mechanical profile of sterilized natural bone in a similar configuration--that of the Cloward plug dowel.

MATERIALS AND METHODS

The material used in this study is an experimental artificial bone graft manufactured and supplied by the U.S. Surgical Corporation (Norwalk, CT).

Identified by the name Hard Tissue Replacement®, or more commonly HTR®, this material is the result of a patented process which envelopes a hydrophobic inner core (poly methylmethacrylate or PMMA) with a hydrophilic shell (poly hydroxyethyl methacrylate or PHEMA). The result of this procedure is a myriad of beads in varying sizes, each with a PMMA core and PHEMA outer shell. The beads can be sorted according to mesh size or left as a random mix. The material can be packed into cavitations in bony tissue as loose beads or heat molded into varying shapes and used as a solid graft. This study used material which had been segregated loosely into two main bead sizes: 20/24 mesh and 30/40 mesh. The tests were performed using HTR® which had been molded into dowel shapes (Figure 3).

The mechanical testing of this material was done in conjunction with an implant study using a Cloward anterior approach in large (> 50 pounds) mongrel dogs. The goal of the implant study was to determine if bone would grow into the HTR®; however, prior to the first implantation it was clear that a great deal of information regarding this material would be necessary.

FIGURE 3: HTR® cloward dowels of varying sizes.

To gain this preliminary information, varying sizes of HTR® plugs were tested in compression. The purpose of examining a large variety of plugs was to determine any change in mode of failure with varying size. In addition, the assortment of dimensions was deemed necessary following X-ray investigation of canine cervical spines. The results of the radiographic inquiry showed marked variability of canine spines and a lack of predictability of spine size given external characteristics of each dog examined.

Visual inspection of each group of plugs concluded that the HTR® was essentially consistent in a 20% diametric compression throughout the range of sizes. Given this knowledge, the first implant of an HTR® plug was performed.

The initial implantation delineated several differences between canine and human cervical spines which were not apparent during the preliminary protocol research. The horizontal state of the canine cervical spine and the propensity of animals to resume motion almost immediately following surgery created a requirement to stabilize the graft plugs -- a requirement not covered in the original Cloward anterior approach description. The initial modification made was to insert a 0.45 french diameter Kirshner wire (k-wire) through the vertebral body cephalad to the graft and into the HTR® plug. Subsequent implants utilized a new plug shape -- the "stadium" shape -- which was designed to increase the proximity of the plug

with the vertebral bodies (Figure 4). Other changes in testing protocol, such as state of graft hydration, were developed following failure of implanted grafts.

The data which was collected during the preliminary phases was used to modify and improve the implantation protocol, and was not analyzed or used in statistical comparisons. Table 1 lists the varying configurations tested initially in conjuction with the implantation study. Note that all testing was done at identical strain rates and at room temperature.

Additional experimentation included the following tests:

1. A group of grafts was subjected to vertical axis compression in an effort to determine the corresponding expansion of the diameter of each plug. This information was to be used to calculate a Poisson's ratio of HTR®.

2. A study involving the ability of HTR® to withstand cyclic loads was attempted in an effort to simulate cyclic loading patterns within canine cervical spines during physiologic load bearing. 13 x 10 mm "stadium" shaped plugs were soaked in lactated Ringers solution for a minimum of 2 hours prior to testing. Two hours was chosen following experimental protocol used for natural bone graft (29). Each plug was then secured within the testing grips and a k-wire was inserted, following the implant study.

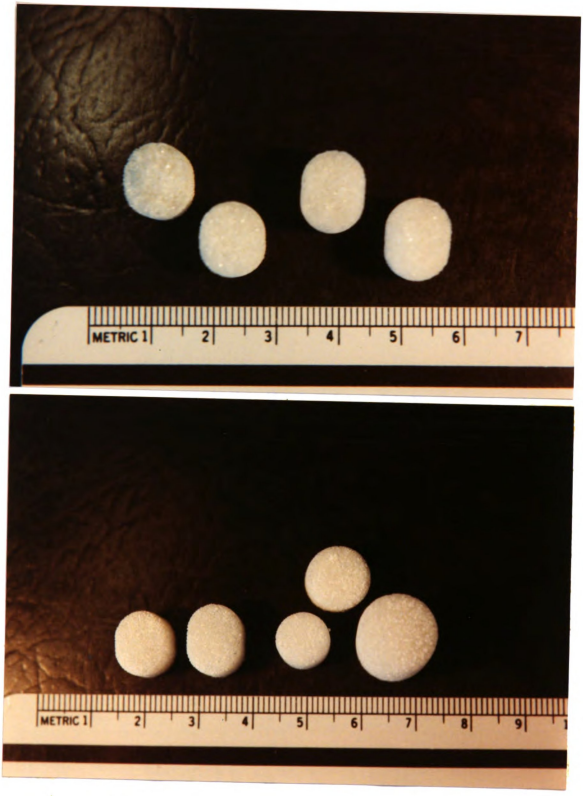


FIGURE 4: "Stadium" shaped cloward dowels (left) and traditional round dowels.

Plug size	DEFORMATION[a] Type	Amount	Hydration
14 mm dia x 20 mm	vertical axis	10% (2 mm)	none
14 mm dia x 20 mm	vertical axis	5% (1 mm)	none
10 mm dia x 10 mm	diametric axis	10% (1 mm)	none
12 mm dia x 10 mm	diametric axis	20% (2.4 mm)	none
12 mm dia x 10 mm	diametric axis	20% (2.4 mm)	2 hours lactated Ringer's soln
12 mm dia x 10 mm[b]	diametric axis	20% (12.4 mm)	none
12 x 10 mm "stadium"[c] x 10 mm	12 mm stadium axis	16.67% (2.0 mm)	2 hours lactated Ringer's soln
13 x 10 mm "stadium" x 10 mm	13 mm stadium axis	15.38% (2.0 mm)	2 hours lactated Ringer's soln

a) All compressions were completed using a 10 second ramp time at room temperature.
b) Kirshner wires (K-wires) were inserted using an electric drill, and were placed at approximately 45° from horizontal, following protocol from the implant study.
c) Figure 4

TABLE 1: Variables included in primary testing.

The first cyclic test used repeated deformations of a specific magnitude. 2.0 mm, following the criteria used in the single ramp tests, was selected as the deformation that the plug was to undergo on a repeated basis for 2 hours.

The second cyclic test was done under load-control conditions, subjecting the plug to loads of not more than 150 lb over a two hour period. The load of 150 lb was arbitrarily chosen based on a combination of the minimal acceptable load needed for human cervical spine graft (1500 N (28)) and the knowledge that the loads generated by dogs within the cervical spine was not expected to be as great as those loads generated within human spines.

3. An experiment to determine the ability of HTR® to absorb fluid was also completed. Prior to this test, a time of 2 hours had been selected as the minimum amount of time required to absorb a maximal amount of fluid, based on results which show the time required by lyophilized natural bone to rehydrate is 2 hours (29). The importance of this was seen after a brief experiment comparing plugs that were "dry" with those that had soaked for an arbitrary period of time (Figure 5).

Three plugs were isolated with dessicant (Sigma Chemical Corporation, St. Louis, Mo.) for 4 hours and then weighed individually on a Mettler analytical balance. After the weights were recorded, the plugs were each placed in separate jars of lactated Ringers solution and incubated

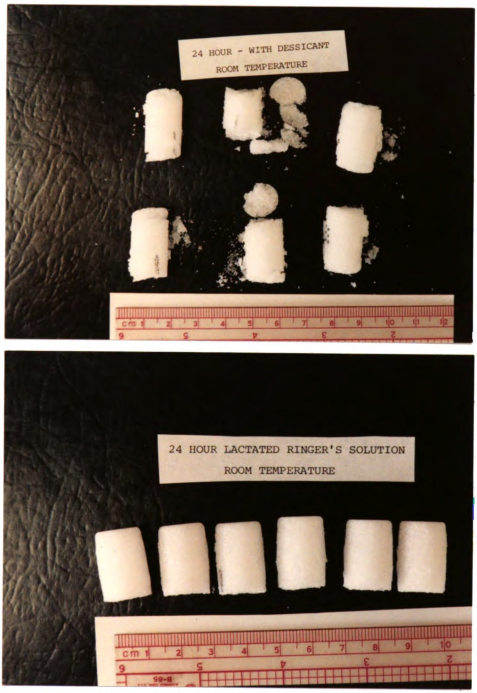


FIGURE 5: Results showing the contrast between modes of failure of "dry" HTR® plugs and those soaked in lactated ringers solution. This graphic demonstration prompted an experiment to analyze how much fluid molded HTR® would absorb.

at 37°C. Subsequent weights were taken at 4, 8, 20, 24, 48 and 72 hours. The weights were graphed to visually estimate the time when the plugs ceased to absorb additional fluid. This was then determined to be the minimum soaking time for HTR® plugs.

4. Axial compression tests to compare stiffness at varying deformation rates:

Fifty-four plugs measuring 14 mm x 20 mm length were randomly divided into three groups. Each group was placed into a different environmental condition: a) exposed to room air at room temperature (21°C), b) hydrated for 24 hours in lactated Ringers solution at room temperature, and c) hydrated for 24 hours at simulated body temperature (37°C). All plugs were returned to room temperature before testing and all tests were run at room temperature. Prior to compression, silicone vacuum grease was applied to the ends of each plug to eliminate end effects, such as barrelling, caused by friction.

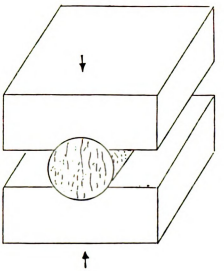
Six plugs from each condition were tested at three different constant strain rates. Each plug was deformed 1.25 mm or 6.25%. The initial strain rate was 0.625%/sec. Subsequent strain rates tested were 10 times the initial rate or 6.25%/sec, and 20 times the initial rate or 12.5%/sec. The unloading pattern was not recorded.

5. A final experiment was performed to mechanically compare HTR® dowels to natural bone graft. Information regarding testing protocol, size of the natural

bone dowels and results for comparison were taken from studies of the strength of bone dowels following various sterilization techniques (21, 29).

Eighteen plugs of HTR® which had been manufactured in a single lot were used in this study. Each plug was first weighed on a Mettler analytical balance and then measured for maximum and minimum diameters and length. The manufactured size was 14 mm diameter X 20 mm length; however, all plugs showed some variability in size. Nine plugs were placed in covered jars containing lactated Ringers solution and nine plugs were isolated in covered glass jars with dessicant. Three "wet" plugs and three "dry" plugs were incubated at 37°C; the remaining plugs were kept at room temperature. The plugs were left for 24 hours--the minimum time required for HTR® to equilibrate in fluid. After 24 hours, the plugs incubated at 37°C were allowed to return to room temperature, and all plugs were then subjected to 20% (2.8 mm) diametric compression over 10 sec. along the greatest measured diameter.

All of the diametric tests described above were completed using equipment which simulated the loading produced in an in-vivo specimen; that is, each plug was loaded between two grips representing vertebral bodies in a vertical position (Figure 6). All test grips were constructed of stainless steel. The tests to determine axial compression modulus were completed using stainless



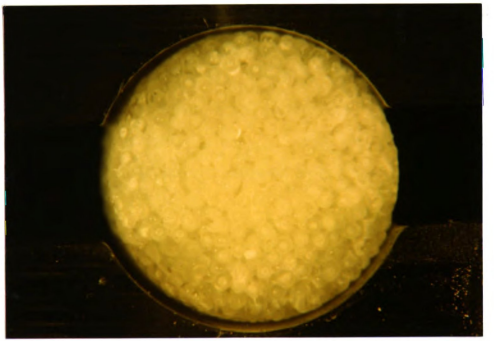


FIGURE 6: HTR® plug within grips representing vertebral bodies.

steel plates, and were not modelled after an anatomical configuration.

The tests were run on an Instron Servohydraulic materials testing machine. All except one of the testing protocols required stroke control to be used; the exception was the cyclic test performed under load control. Load and deformation data were recorded on a Nicolet digital oscilloscope and stored as voltage measurements on floppy disks. The data was then transferred to an IBM PC Clone and converted to load-deformation curves (Figure 7).

From the load-deformation curves, the stiffness and yield load of each specimen was determined. Stiffness was defined as the slope of the linear portion of the curves. Yield load was defined as the intersection of a line offset 2% from the linear portion of the curve with the curve. Peak load was determined by converting the voltage value corresponding to the maximum point on the Nicolet load curve to Newtons (Figure 8).

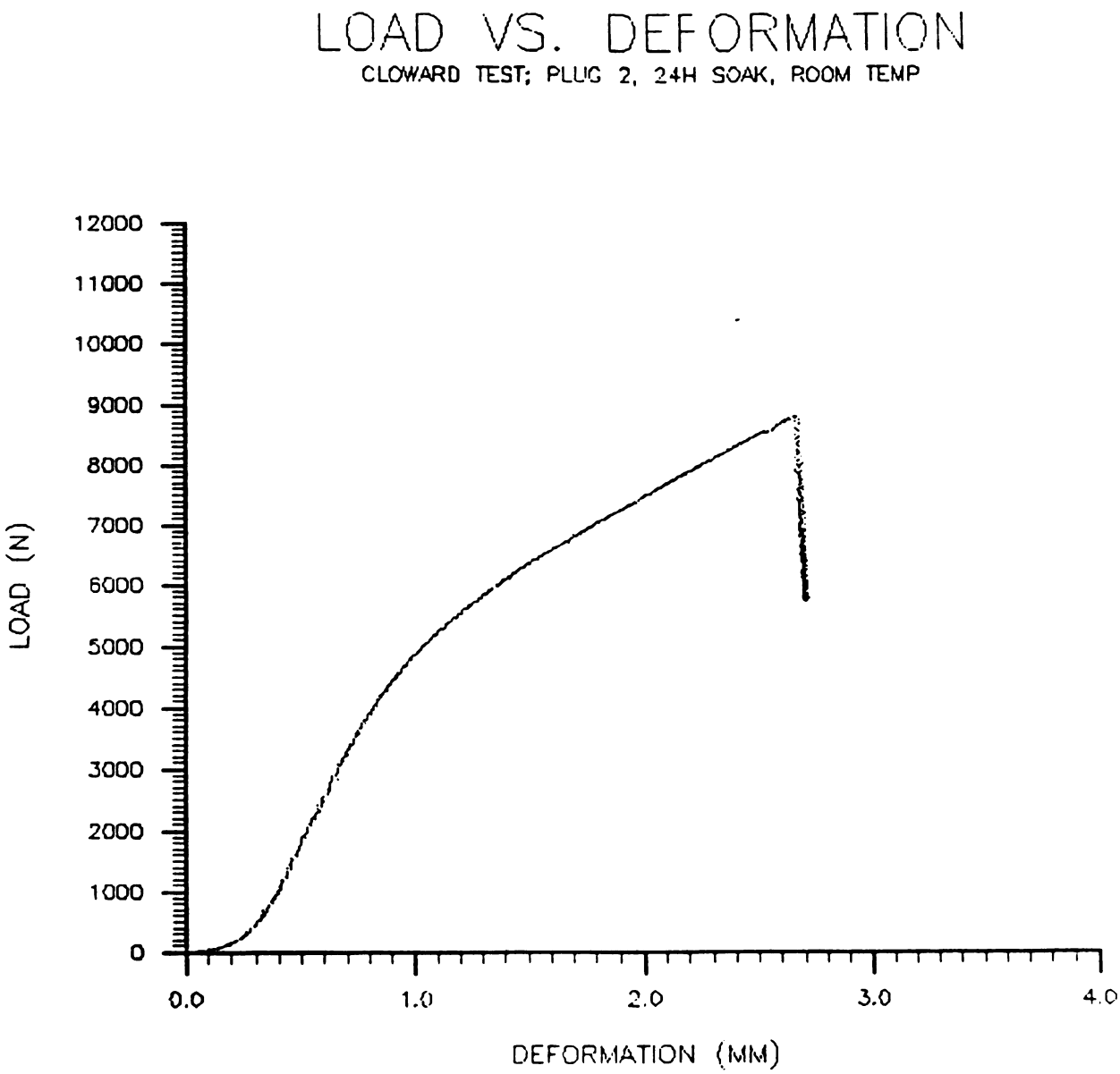


FIGURE 7: Typical load-deformation curve generated during compression of HTR®.

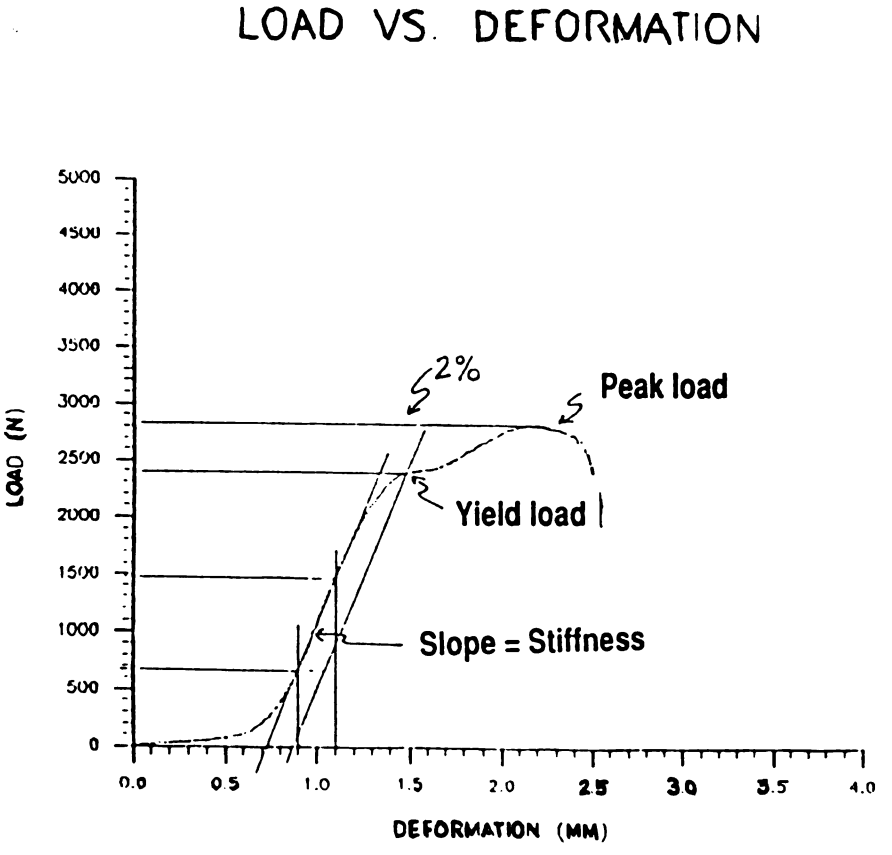


FIGURE 8: Typical load-deformation curve showing method of calculating stiffness and yield load, as well as location of peak load.

RESULTS

1. Poisson's ratio: The plugs were seen to compress in a variable fashion during a minimal sustained axial load (Figure 9). Given this variability, it was not possible to accurately measure resultant diametric expansion nor to calculate a Poisson's ratio for this material using this method.

2. Cyclic testing: The first plug, subjected to repeated deformations of specific magnitude (2 mm) for two hours, crumbled shortly after one hour of testing. The second plug, tested under load-control conditions and exposed to loads of not more than 150 lbs over a two hour period, was intact at the end of the testing period and showed no sign of failure or fracture.

3. Fluid absorption: The plugs continually absorbed fluid (indicated by an increasing weight) until 24 hours had elapsed. At 72 hours past the start of fluid immersion, the weight of each plug was not significantly different from that of 24 hours (Figure 10).

4. Axial compression: The plugs which were designated as "dry" were able to withstand a higher total load than the groups of wet conditioned plugs at each of the different strain rates. There is also evidence that higher loads were obtained at the strain rate of ten times that of the intitial strain rate. This pattern does not continue as the strain rate increases to twenty times the original rate.

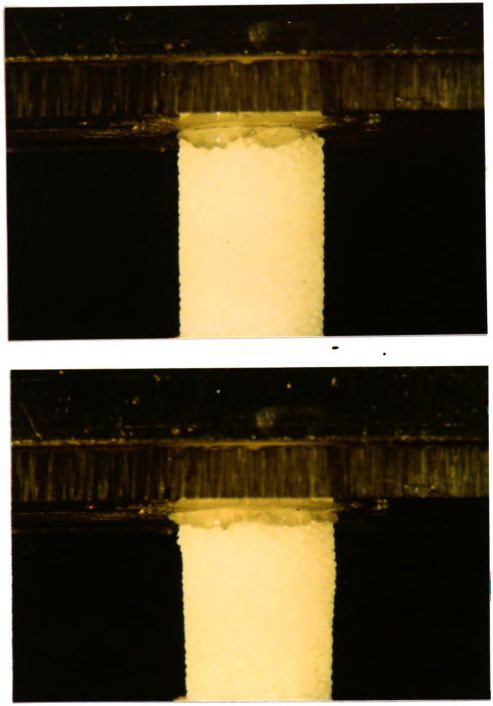


FIGURE 9: Variability seen during axial compression.

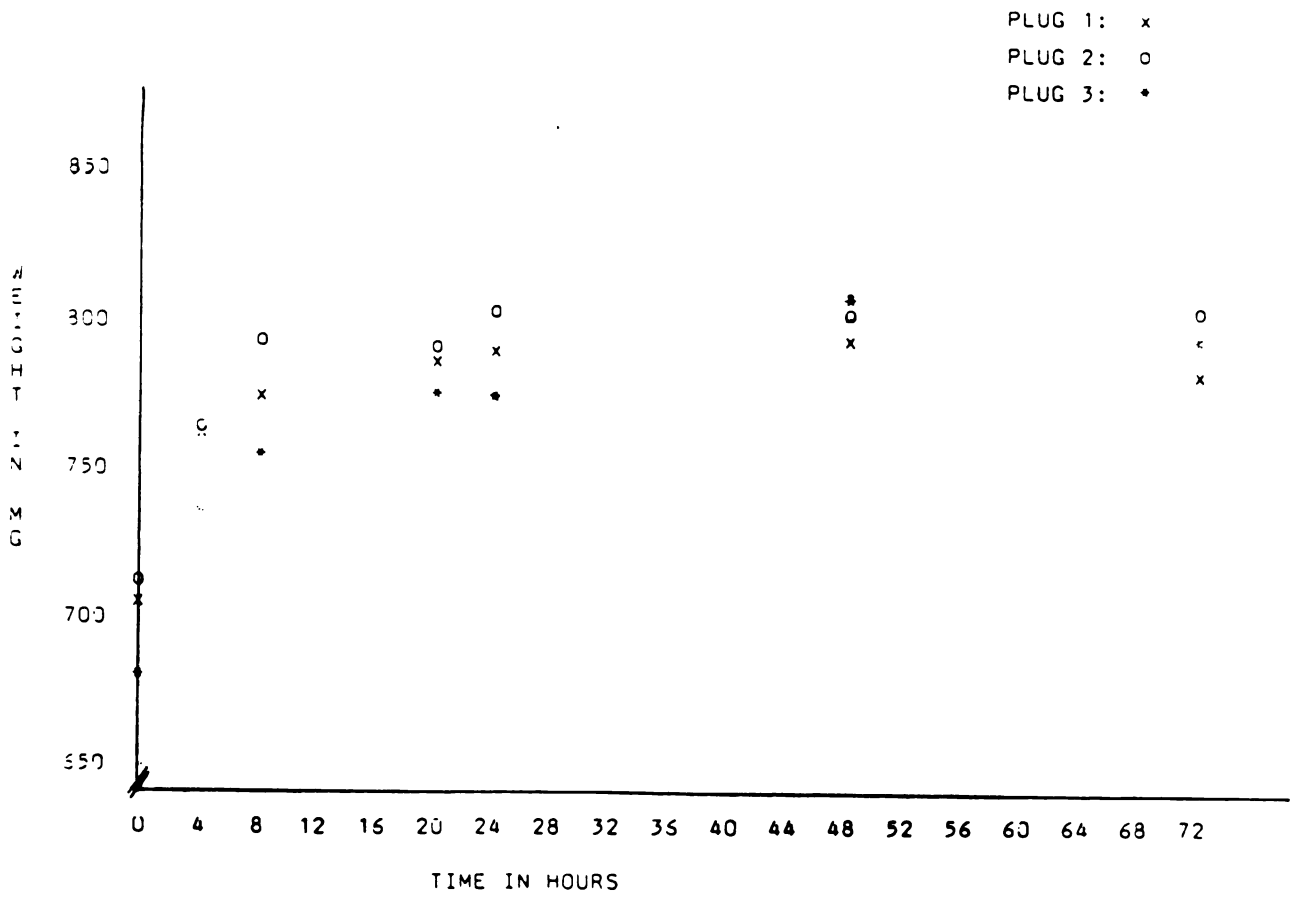


FIGURE 10: Graphic results of weighing experiment. All plugs were kept at 37°C. Plugs were not allowed to return to room temperature prior to weighing.

TIME (HOURS)	PLUG 1	PLUG 2	PLUG 3
0	704.0 mg	712.5 mg	681.1 mg
4	763.1 mg	764.7 mg	737.9 mg
8	774.3 mg	793.3 mg	751.1 mg
20	783.8 mg	792.5 mg	774.5 mg
24	790.4 mg	801.8 mg	773.4 mg
48	793.2 mg	801.3 mg	806.7 mg
72	778.6 mg	807.8 mg	793.8 mg

TABLE 2: Results of weighing experiment.

A material modus value (E) was calculated from the values of stress and strain. Under all conditions, it can be seen that the moduli values obtained for strain rates of ten and twenty times the initial rate are similar to each other, but much larger than the values calculated for the initial strain rate (Figure 11).

5. Comparison to natural bone: All plugs behaved in a manner consistent with that of cancellous bone; that is, each sample demonstrated an initial linear elasticity, a plastic yield point and a final increased resistance to load when plotted on a typical load-deformation curve.

Mean yield load values obtained for each specimen averaged from 74 -190% higher than corresponding yield loads obtained for fresh bone dowels. Similarly, mean peak load values ranged from 195 - 216% higher than the highest reported value for the natural dowels, while mean stiffness values averaged 31% higher than the average reported value for natural bone (21). Paired t-tests indicate that these values are significant at p=.001 (Figure 12).

All HTR® grafts which were implanted within canine cervical spines showed signs of breakage or failure in the plugs; however, no dog showed neurologic deficit, indicating that even after breaking, the material retained some strength. In addition, all plugs which were examined after eight weeks of implantation showed signs of bony ingrowth into the graft material (Figures 13, 14 and 15).

MODULI VALUES FOR EACH CONDITION

N/mm^2

		Initial strain rate	10 x initial rate	20 x initial rate
Dry Samples	Mean E	369	442	432
	σ	50.5	37.3	35.3
Wet Samples (21.0^oC)	Mean E	279	325	336
	σ	29.6	15.5	25.9
Wet Samples (37.0^oC)	Mean E	254	290	299
	σ	30	25.1	33.8

σ denotes standard deviation

FIGURE 11: Moduli values (N/mm^2) calculated after axial compression. Temperature values refer to pre-test conditions; all tests were run at room temperature.

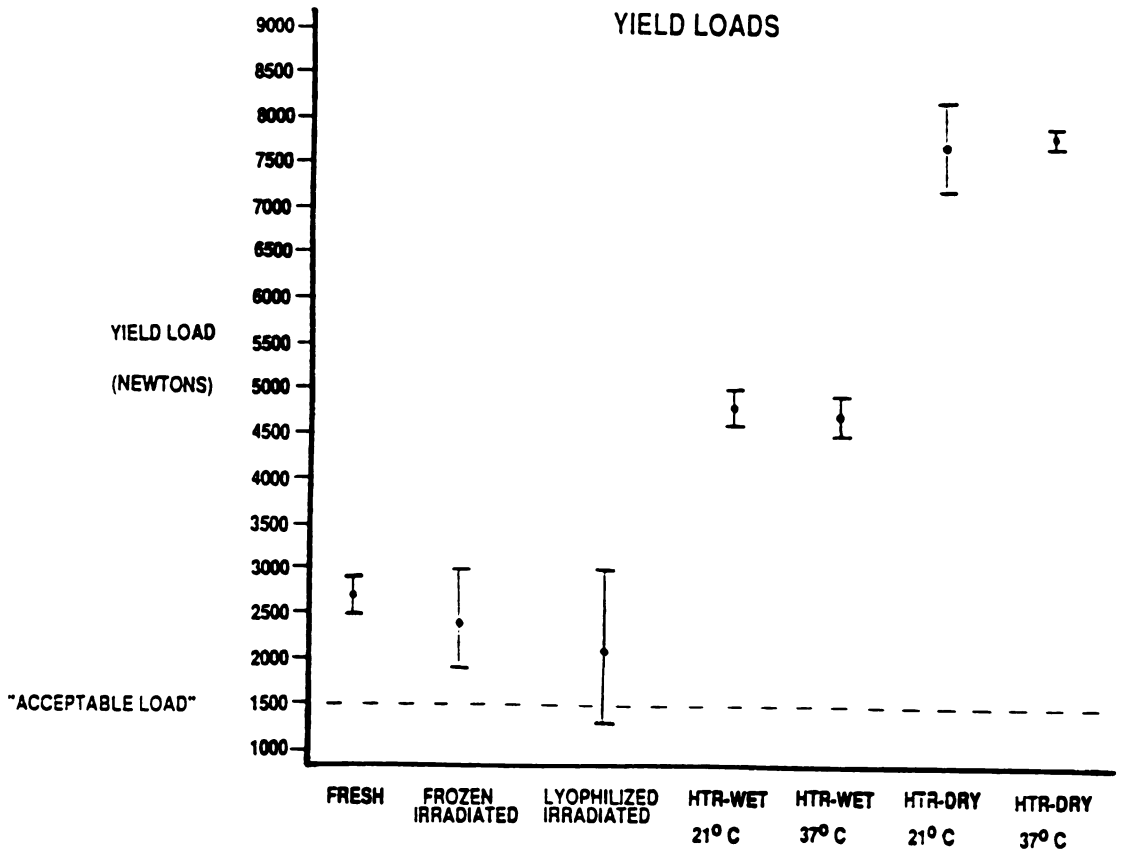


FIGURE 12: Yield loads of natural bone and HTR® grafts in diametric compression. All tests were run at identical strain rates and at room temperature. Descriptions listed are pre-test conditions.

GROUP	SPECIMEN NUMBER	YIELD LOAD	PEAK LOAD	STIFFNESS
Lactated Ringer's Solution - 24 H Room Temperature	1	4700 N	8950 N	7500 N/mm
	2	4500 N	8650 N	7667 N/mm
	3	5000 N	9750 N	8000 N/mm
	4	5200 N	9750 N	8667 N/mm
	5	5000 N	8800 N	8000 N/mm
	6	4730 N	8600 N	7000 N/mm
Lactated Ringer's Solution - 24 H 37°C	1	4500 N	9300 N	8000 N/mm
	2	5000 N	9100 N	7666 N/mm
	3	4600 N	9000 N	7333 N/mm
Dessicant - 24 H Room Temperature	1	7550 N	9600 N	10333 N/mm
	2	7000 N	9750 N	10667 N/mm
	3	7900 N	9500 N	10000 N/mm
	4	8250 N	9460 N	11333 N/mm
	5	7500 N	9400 N	9667 N/mm
	6	8300 N	9430 N	12000 N/mm
Dessicant - 24 H 37°C	1	7800 N	8950 N	11333 N/mm
	2	7900 N	8950 N	11667 N/mm
	3	7800 N	8800 N	10667 N/mm

TABLE 3: Mechanical properties of HTR® dowels in diametric compression. Group description refers to pre-testing conditions. All tests were run at room temperature and at identical strain rates following protocol used in natural bone allograft testing.

SPECIMEN NUMBER	YIELD LOAD	PEAK LOAD	STIFFNESS
18687A	2300 N	2509 N	4500 N/mm
18687B	2150 N	2410 N	3600 N/mm
19787A	1840 N	2079 N	5400 N/mm
19787B	1950 N	2016 N	5200 N/mm
20087A	2720 N	3091 N	5650 N/mm
20087B	3110 N	3745 N	5050 N/mm
20187/38A	2150 N	2697 N	4300 N/mm
20187/39B	2400 N	2822 N	4050 N/mm
20587A	2050 N	2182 N	6500 N/mm
20587B	700 N	819 N	1900 N/mm
20887/4A	3400 N	3544 N	4950 N/mm
20887/4B	2600 N	2769 N	5100 N/mm

TABLE 4: Mechanical properties of bone dowels in diametric compression (22).

FIGURE 13: Subgross photomicrograph of fused intervertebral space demonstrating porous HTR®. Note the fracture in the middle of the graft. There is also a sectioned bone pin (middle right region). 1, 2, and 3 refer to zones examined by conventional light microscopy. H&E, 4X.


2
3
1

FIGURE 14: Photomicrograph from Zone 1 of Figure 13. There is an abrupt transition from normal, woven trabecular bone (left) into the pale-staining osteoid growing within the HTR®. H&E, 18X.

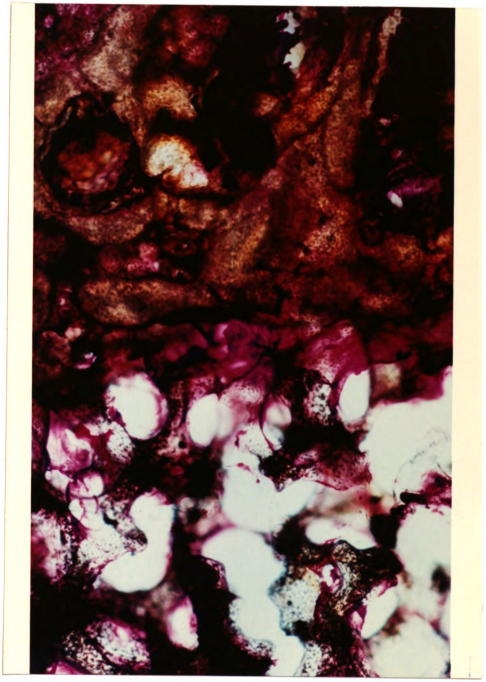
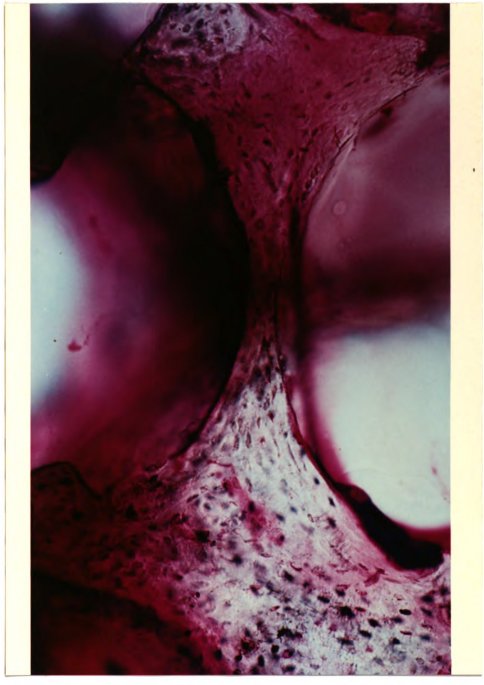


FIGURE 15: Photomicrograph from Zone 1 of Figure 13: Bony trabeculae growing within the porous implant material. There are osteoblasts with rounded nulcei surrounded by an osteoid matrix. H&E, 72X.



DISCUSSION

The results of the in-vitro testing show a great deal of consistency. Why, then, was it impossible to obtain a Poisson's ratio of this material? The most valid explanation is the porosity of this material. When each plug was crushed along its axis, theoretically only the beads nearest the compression arm would have been exposed to the load generated. The pores between the beads would have acted as a "cushion" for the remainder of the plug and absorbed the majority of the compression by simply collapsing. This would explain the deformation seen only nearest the compression arm during the experiments to determine Poisson's ratio.

A second question that must be considered is: Given the alleged identical features of each manufactured group of plugs, why was so much variation seen -- both in visual inspection of the plugs and in plug weights? (This variation was most obvious during the weighing experiment.) One possible explanation is that, given the slight variation in bead sizes within the grafts, there must be a corresponding variation in porosity for each plug. Recall that the manufacturer did not separate bead sizes beyond a crude 20/24 mesh or 30/40 mesh size. This would imply a corresponding "chance" distribution of beads within the molded plugs, leading to a wide variety of dead space among the plugs.

The results of the axial compression tests were as expected: the material stiffened as the strain rate rate increased, and then appeared to begin to level off at a constant stiffness. The "dry" samples were seen to be stiffer in all forms of compression, indicating a greater likelihood of brittle failure, similar to the failure mode seen in natural bone prior to rehydration (29).

Given the variability described above, are the results which show HTR® to be significantly ($p < 0.001$) stronger than natural bone accurate? The author has confidence that the results are correct. In each case of diametric compression the material was deformed to an extent which eliminated all pores between beads and therefore tested only the material itself. By inspection of the raw data (Appendix A), it is possible to see a "knee" or flat portion of each deformation curve prior to the generation of any load on the material. This flat portion is believed to be the collapse of the pore or dead space within each plug, following which is the curve which represents the properties of HTR® accurately.

The results outlined above indicate the HTR® is significantly stronger than natural bone in compressive states. This is desirable during the initial stages of a graft implant when brittle failure is most likely to occur. And, because some grafts can take as long as six months to become fully incorporated, long term strength is a necessity as well (40). HTR® does not undergo

biodegradation within the body, but instead retains its structure (3). Thus, it can be theorized that HTR® will demonstrate long term strength and stability.

HTR® is easily sterilized by common methods without damage to its inherent structure. In addition, HTR® can be kept in a hydrated state indefinitely as, after twenty-four hours, it will absorb no more liquid. This demonstrates an ease of handling and storage which is currently not seen when working with natural bone.

At this time, the standard for grafting material remains natural bone allograft. However, the results described here indicate that the synthetic grafting material known as HTR® appears to be an adequate substitute.

While these in-vitro results show that HTR® is consistently stronger than natural trabecular bone in diametric compression, the parallel implantation studies did not replicate these conclusions. In contrast, the implantation studies frequently met failure due to graft breakage. This was completely unexpected following the in-vitro experiment results.

There are several reasons as to why the grafts may have failed within the in-vivo setting including the fact that the grafts were only tested in compression. Forces within a living being will include torsion and bending (Figure 16), either of which may have contributed to the failures.

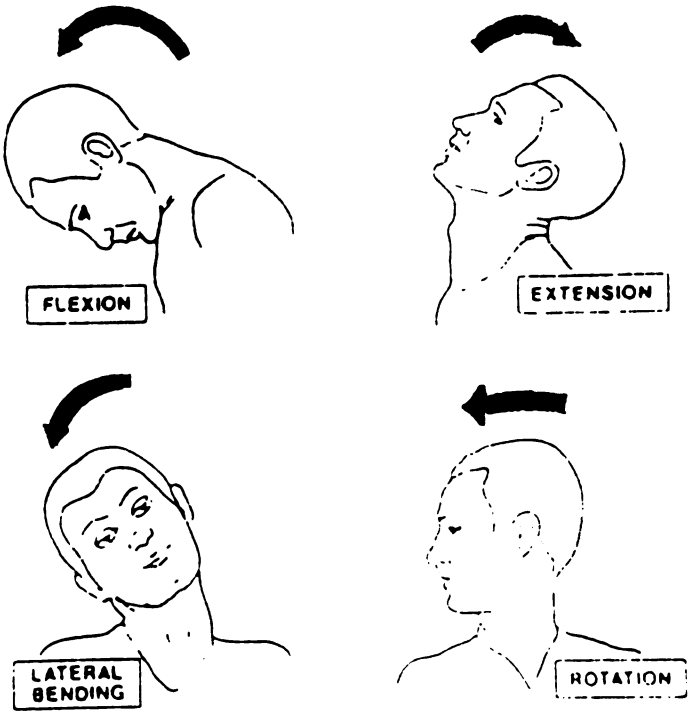


FIGURE 16: Forces acting on the head and neck.

A second reason, perhaps more significant, are the mechanical problems found with the cylindrical shape of the cloward plug as reported by Keblish., et al (25) in 1967. These problems were reported clinically and had enough impact so that at least one major hospital abandoned entirely the Cloward shape in 1964.

There are three main shapes of bone graft used for spinal fusion: cylindrical (Cloward), horseshoe (Smith-Robinson) and strut (Bailey-Badgley) (Figure 17). White, et al (40) studied the load-bearing capabilities of each of these graft shapes immediately following implantation. Their results indicate that the Smith-Robinson horseshoe shaped graft was mechanically strongest. This conclusion is based in part on the shape of the graft -- shown to be strongest -- and in part on the fact that the cortical endplates of the vertebral bodies are not destroyed during implantation of the graft.

Given this information and the results of the research conducted for this thesis, it would appear that HTR® may still succeed in an in-vivo setting. If modifications reflecting the increased strength of the Smith-Robinson graft are coupled with the known compressive strength of HTR®, the result may well be a graft which is strong, easily sterilized, and adaptable. More study is needed to quantify these thoughts; however, as additional information becomes known, it is likely that artificial

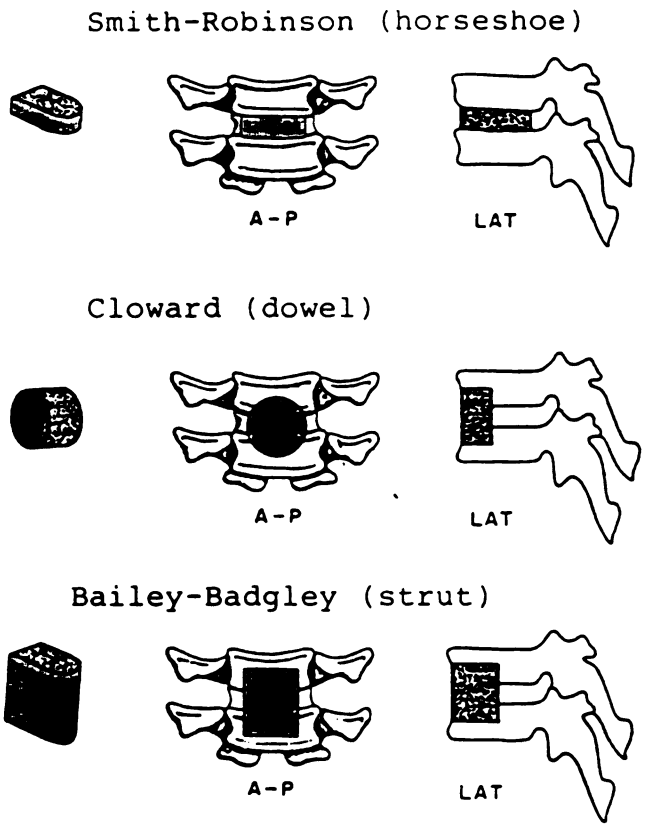


FIGURE 17: Graft shapes used for spinal fusions.

graft will replace natural bone as the standard, guaranteeing sterility and function in a variety of applications.

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APPENDIX A

APPENDIX A: RAW DATA FROM DIAMETRIC COMPRESSION TESTS

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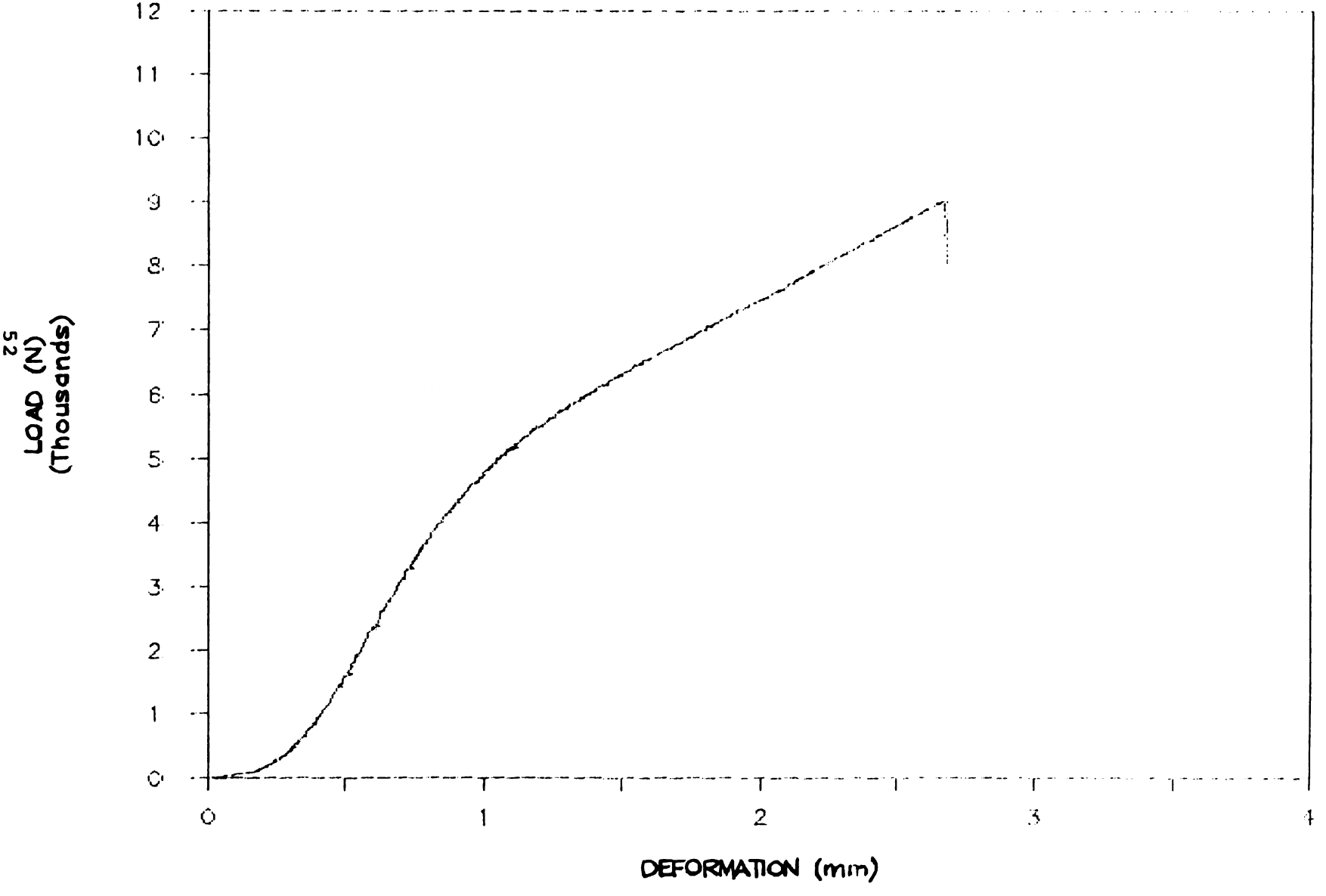

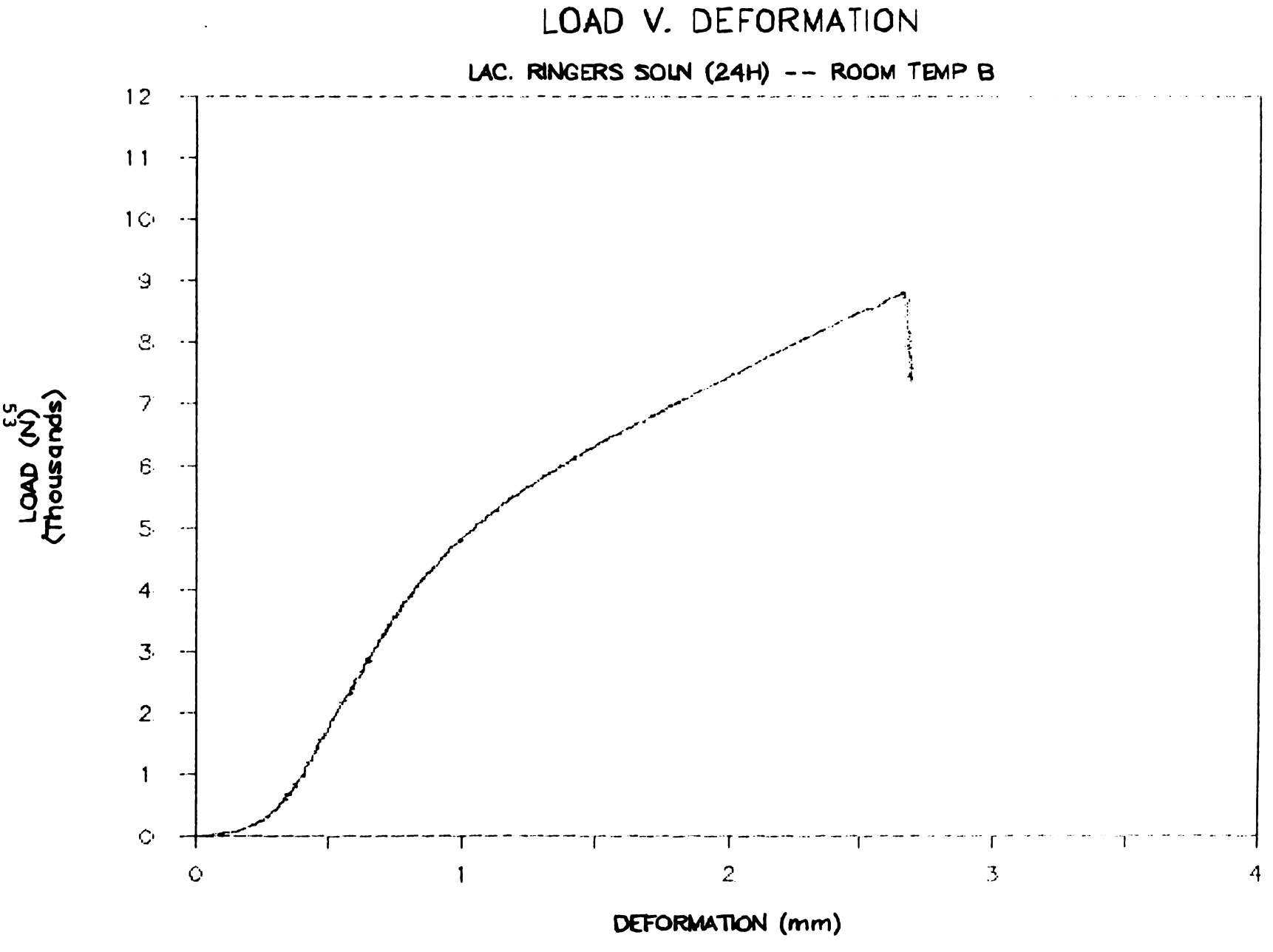
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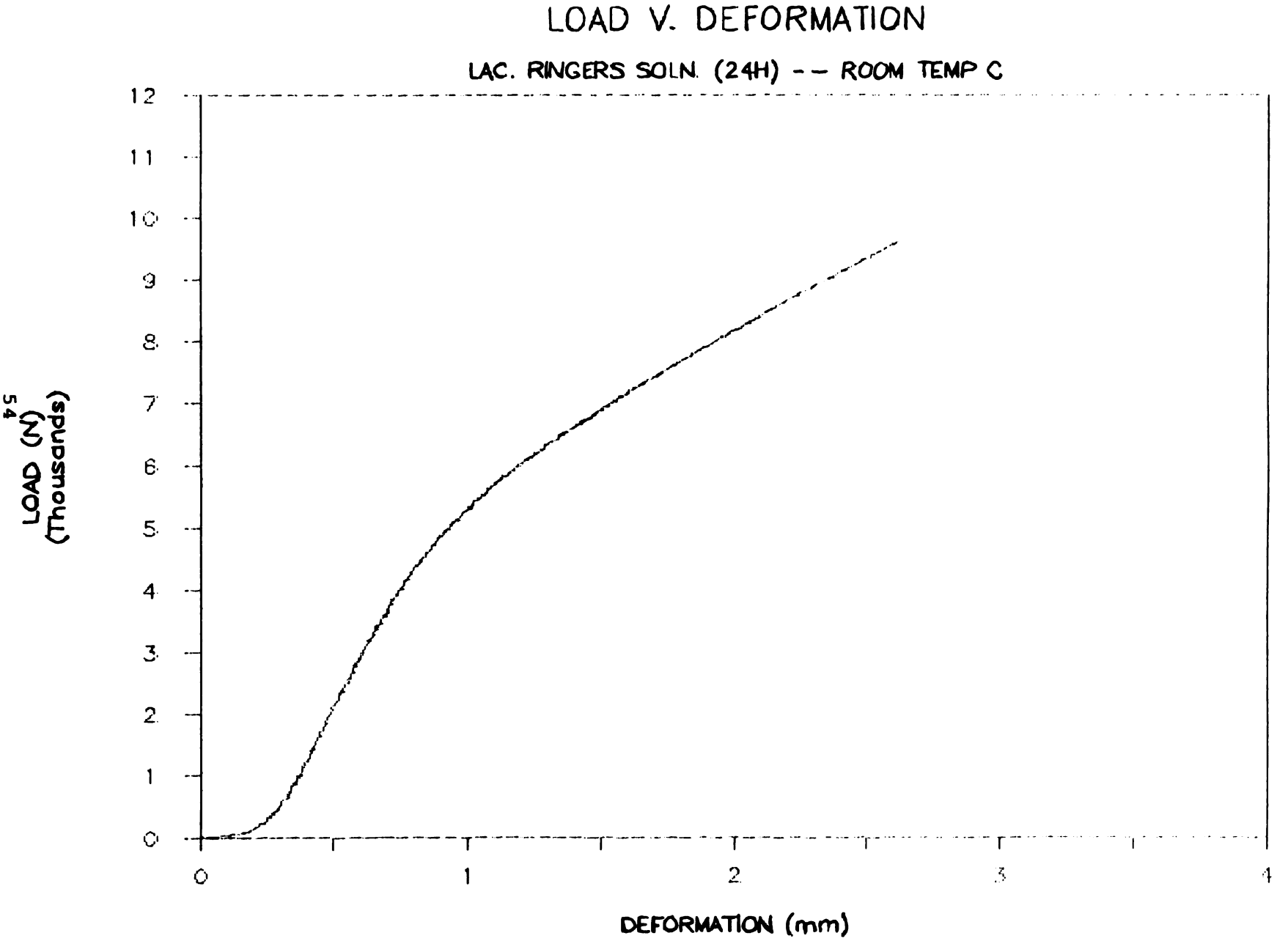
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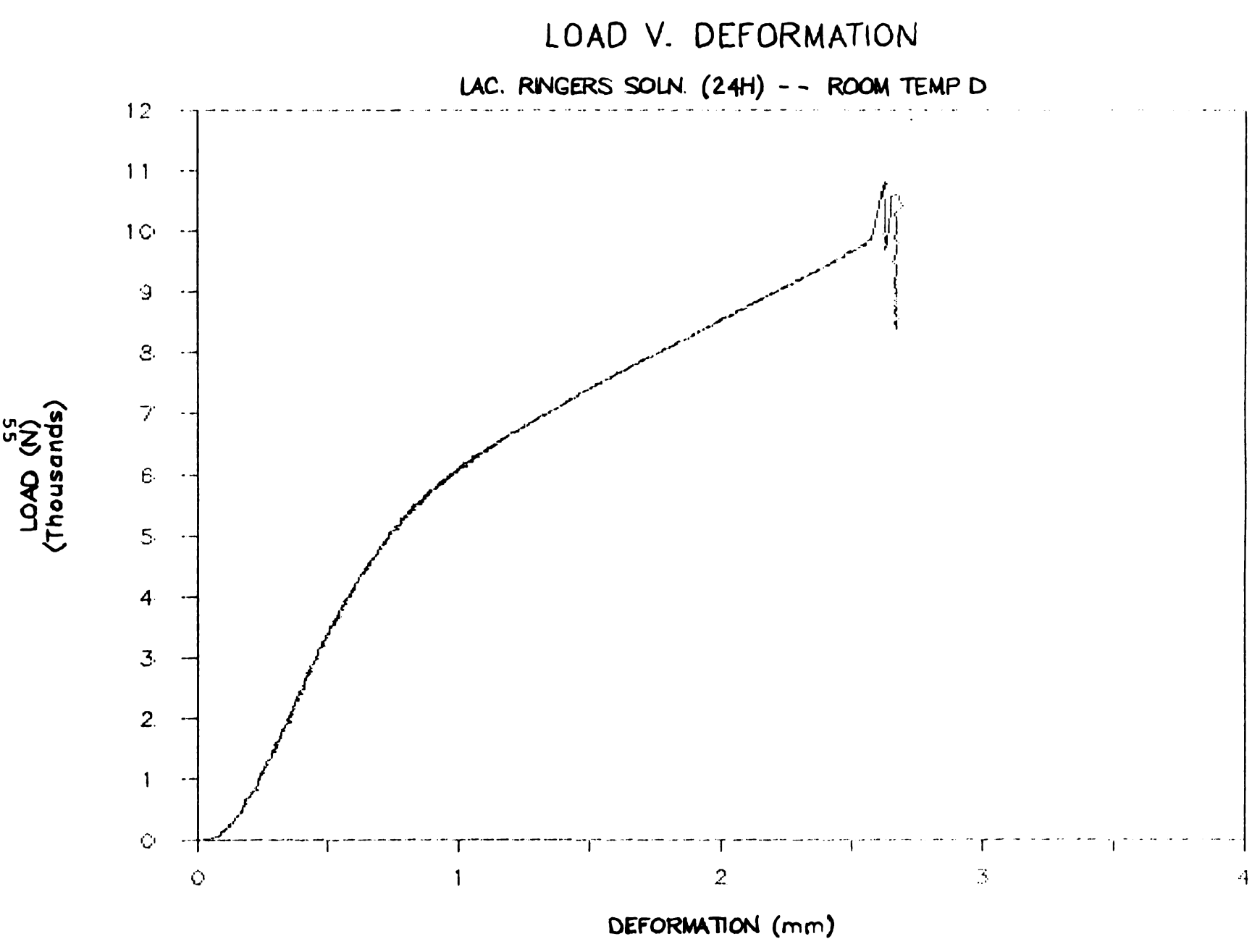
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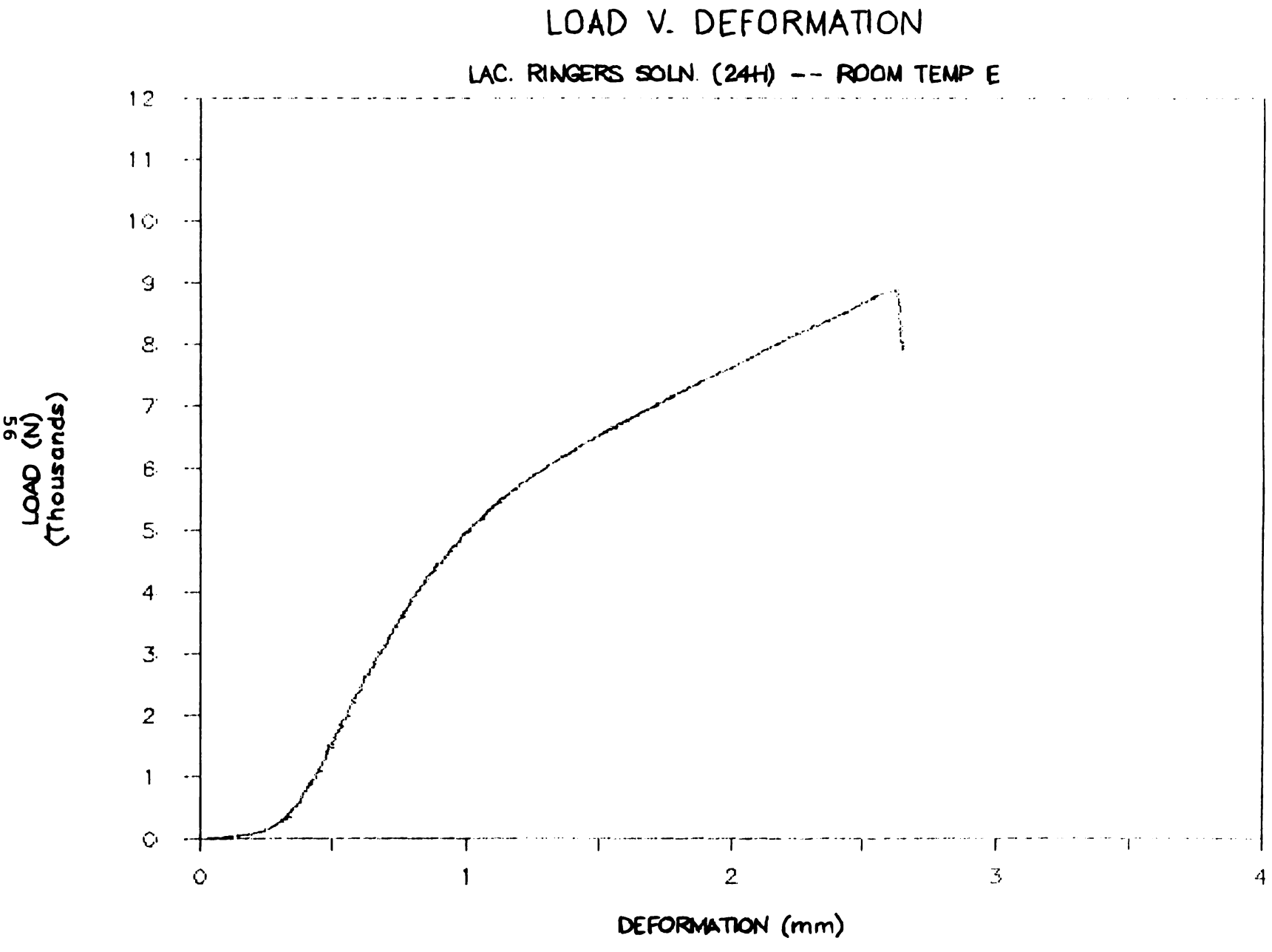
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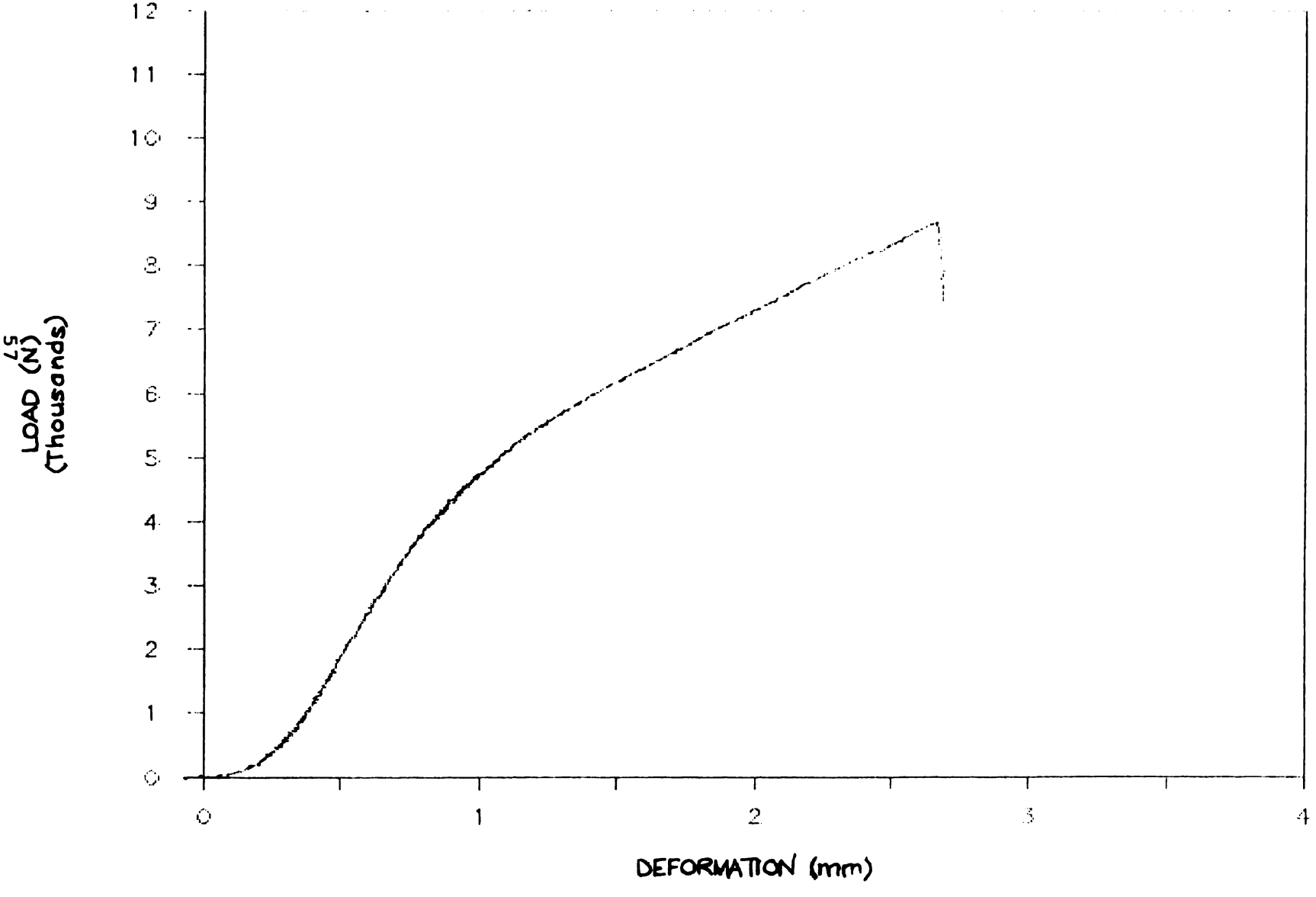

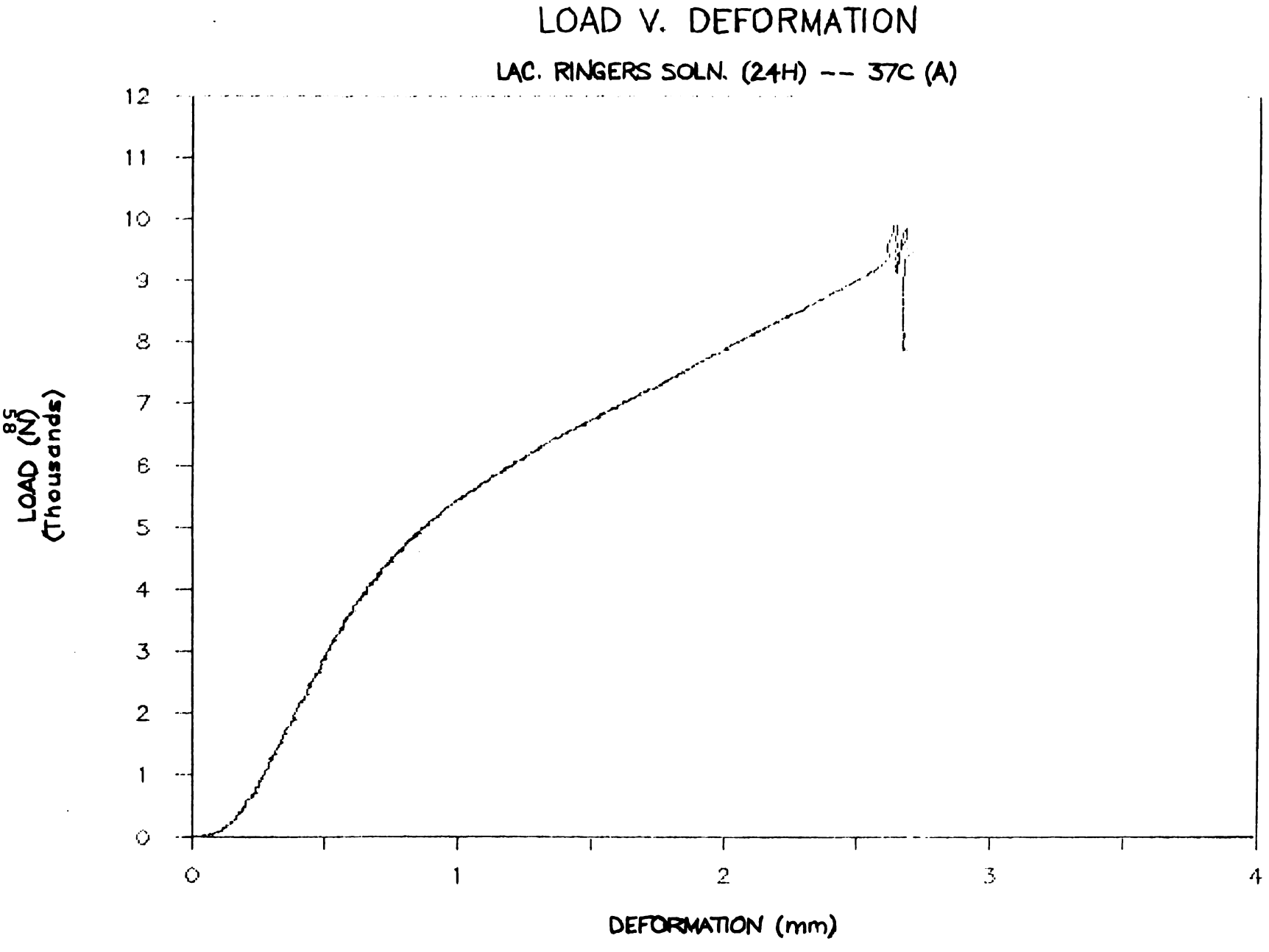
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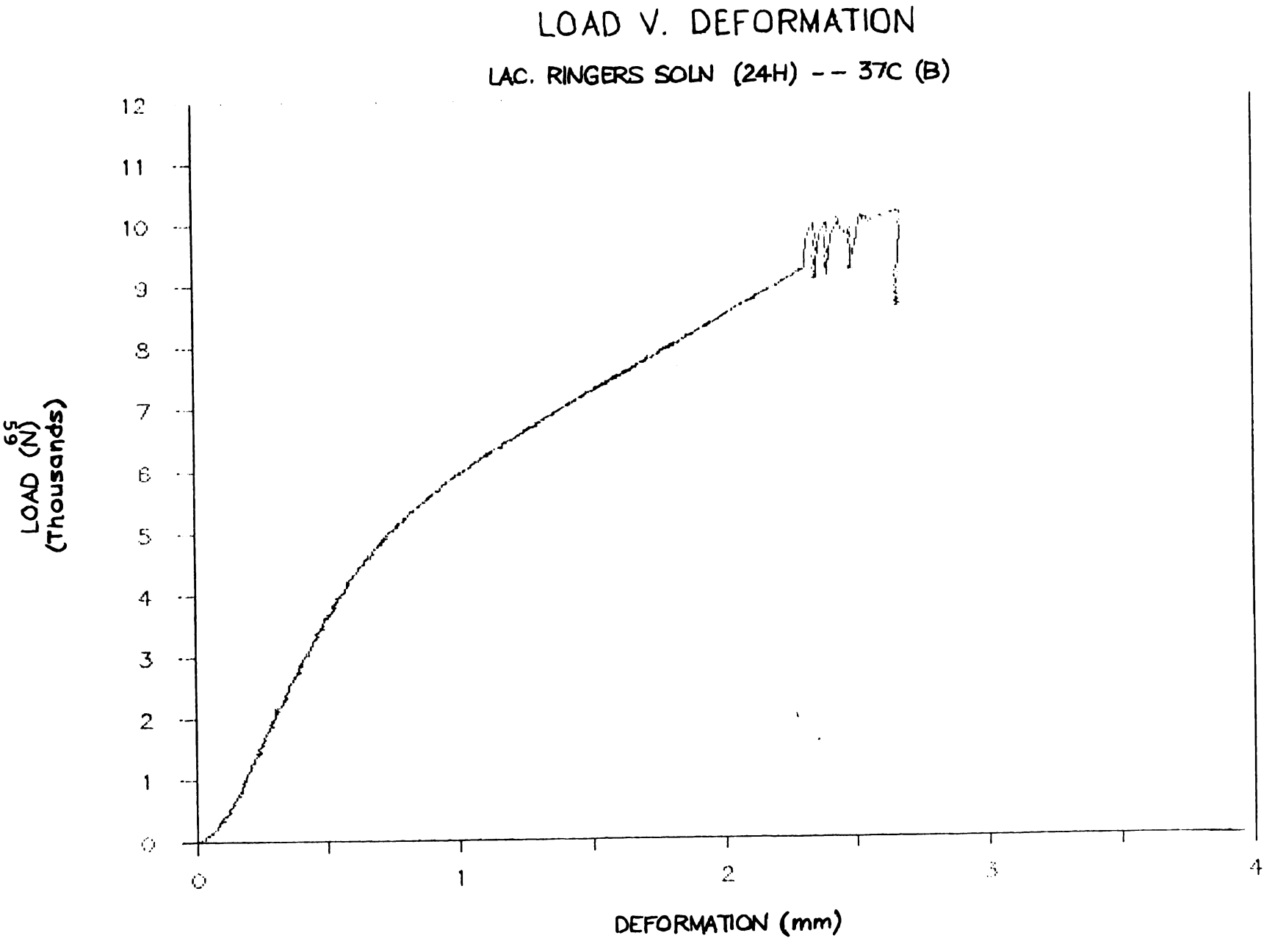
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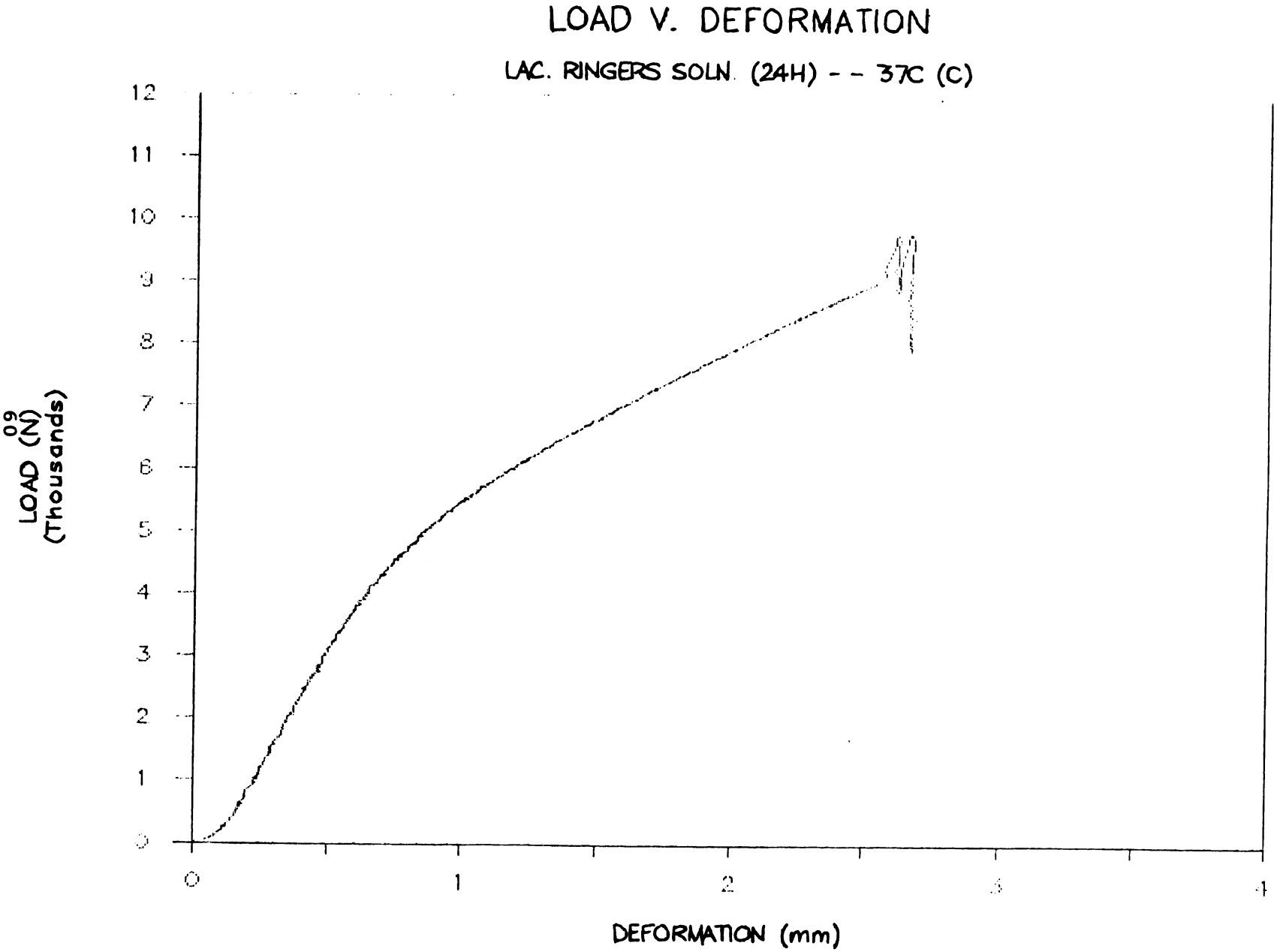
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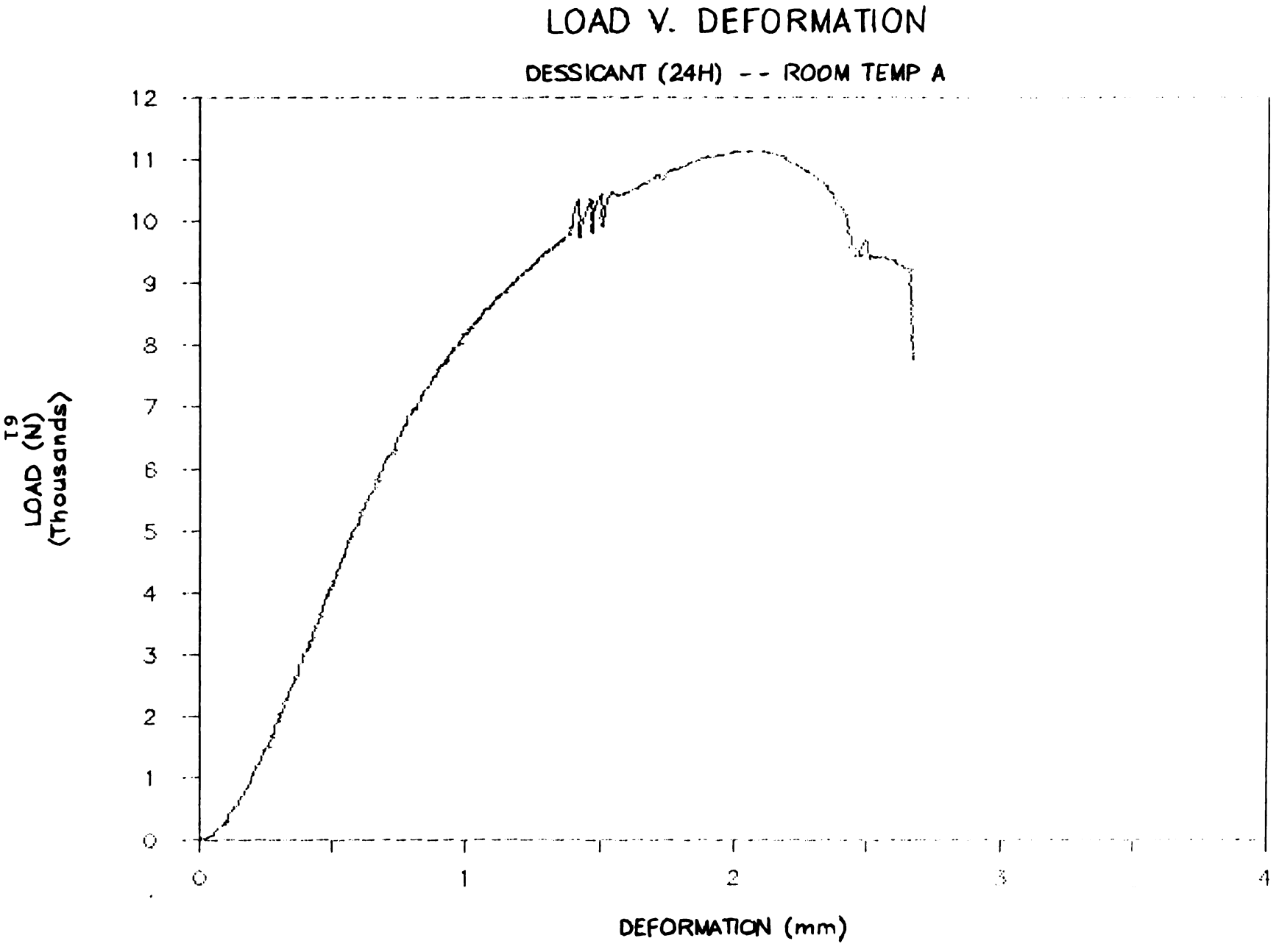
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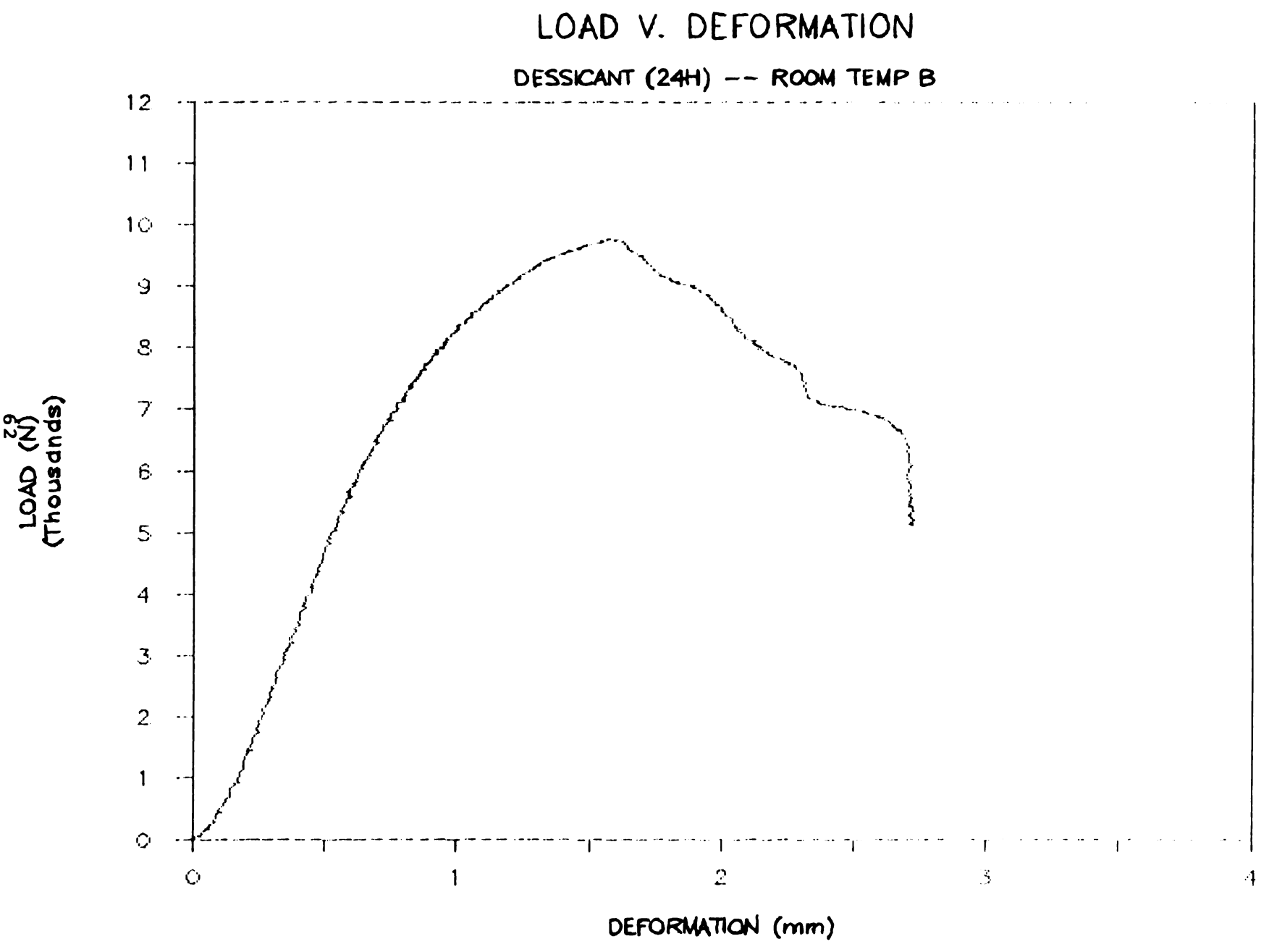
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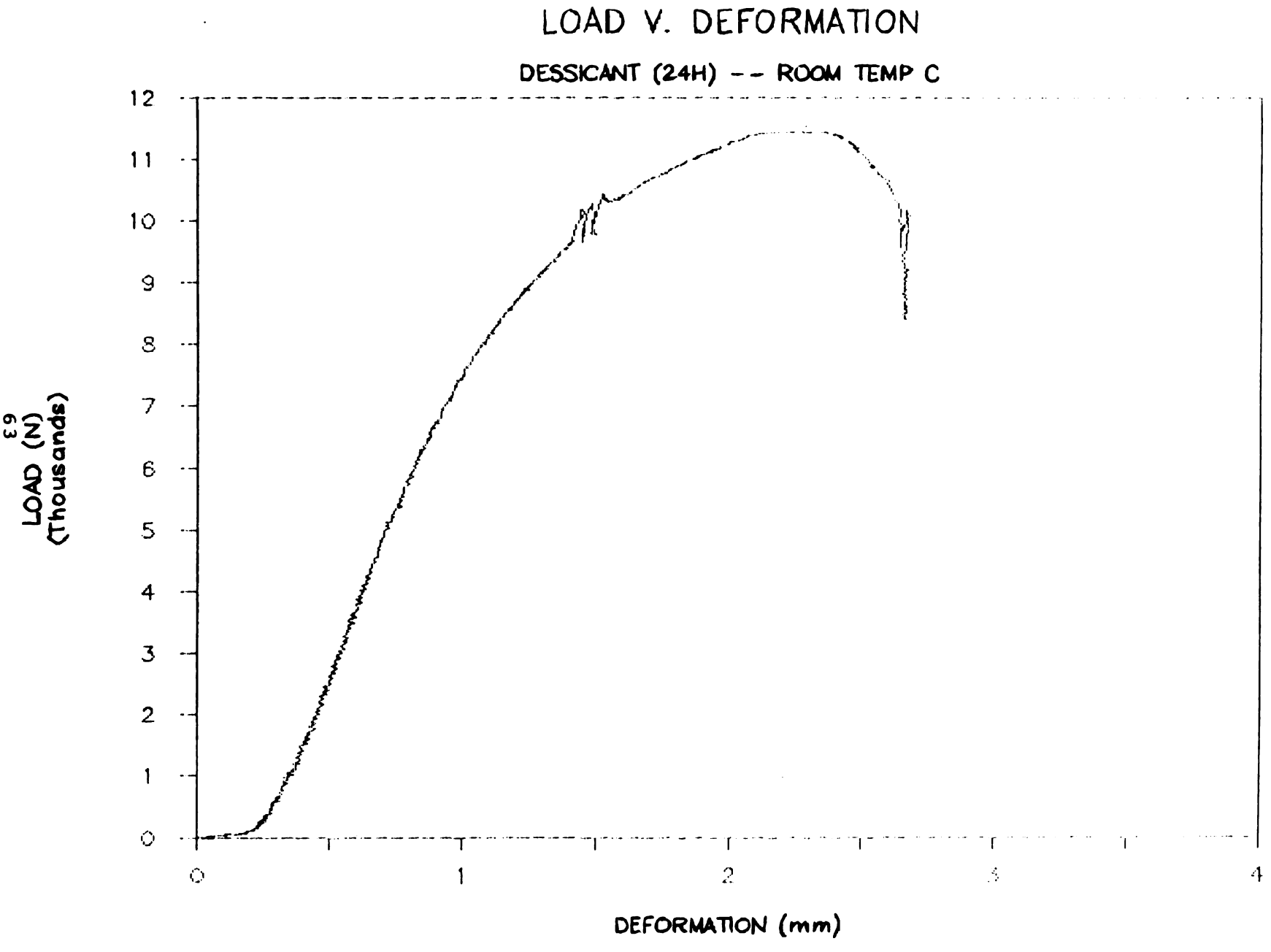
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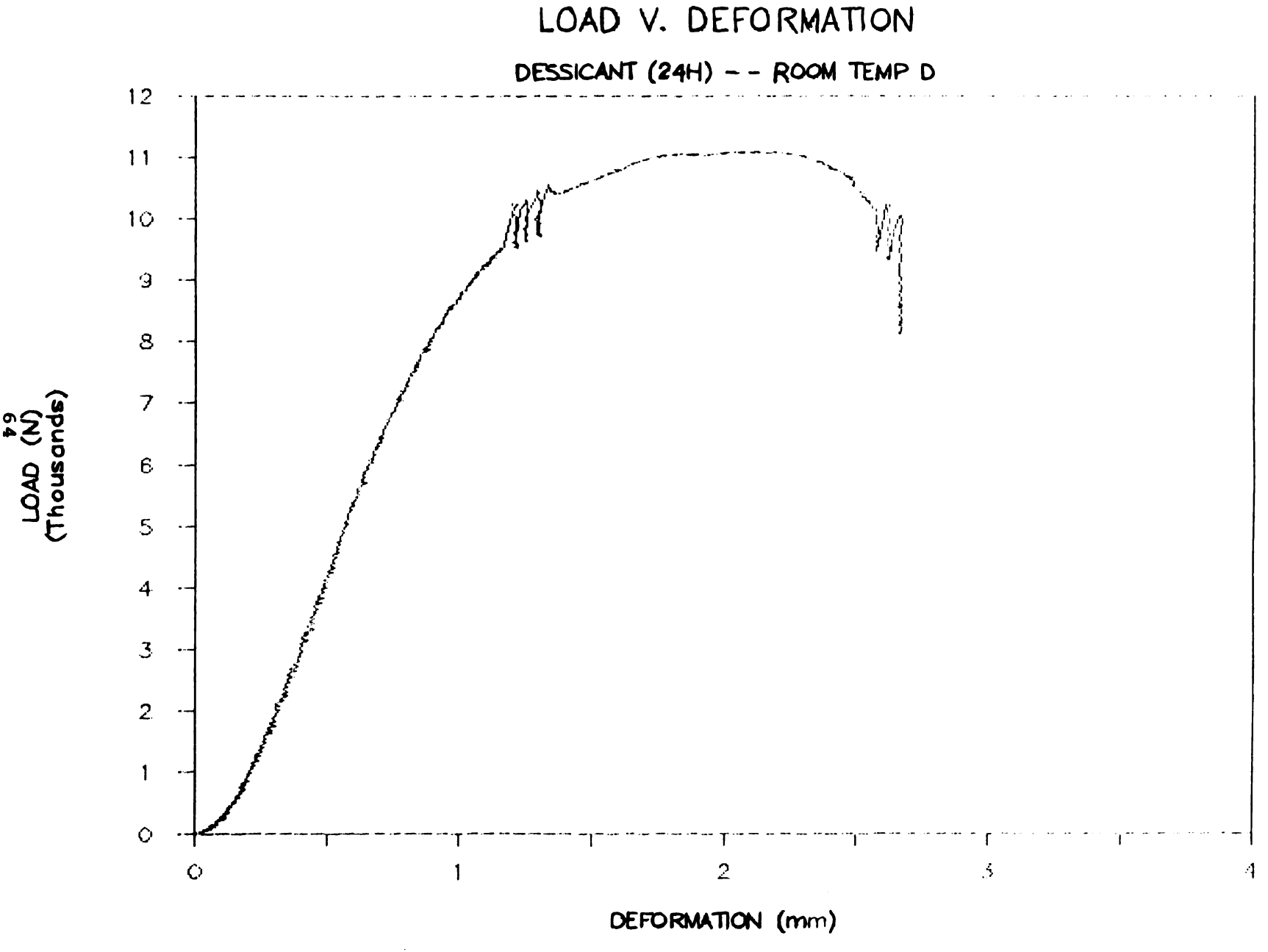
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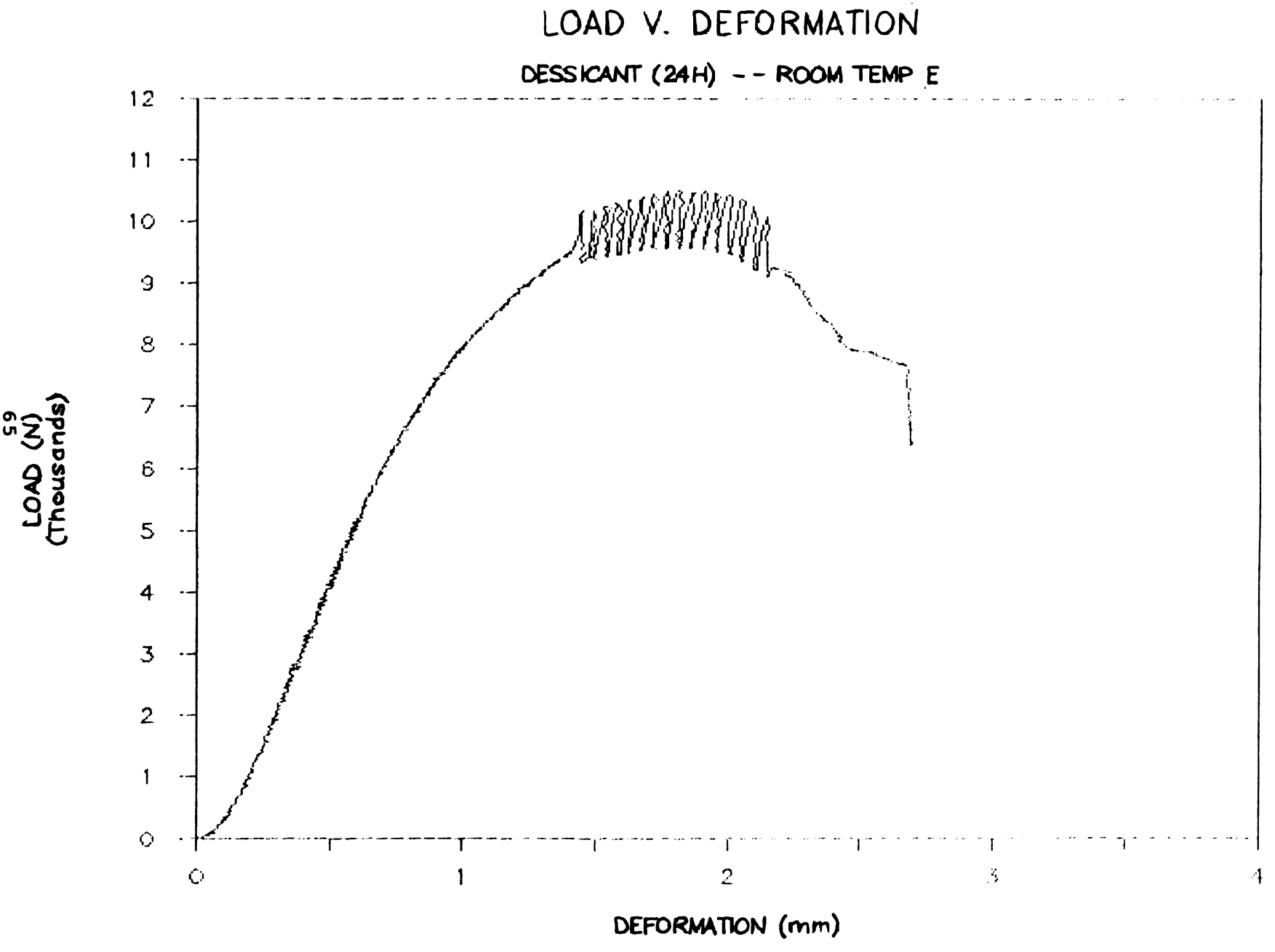
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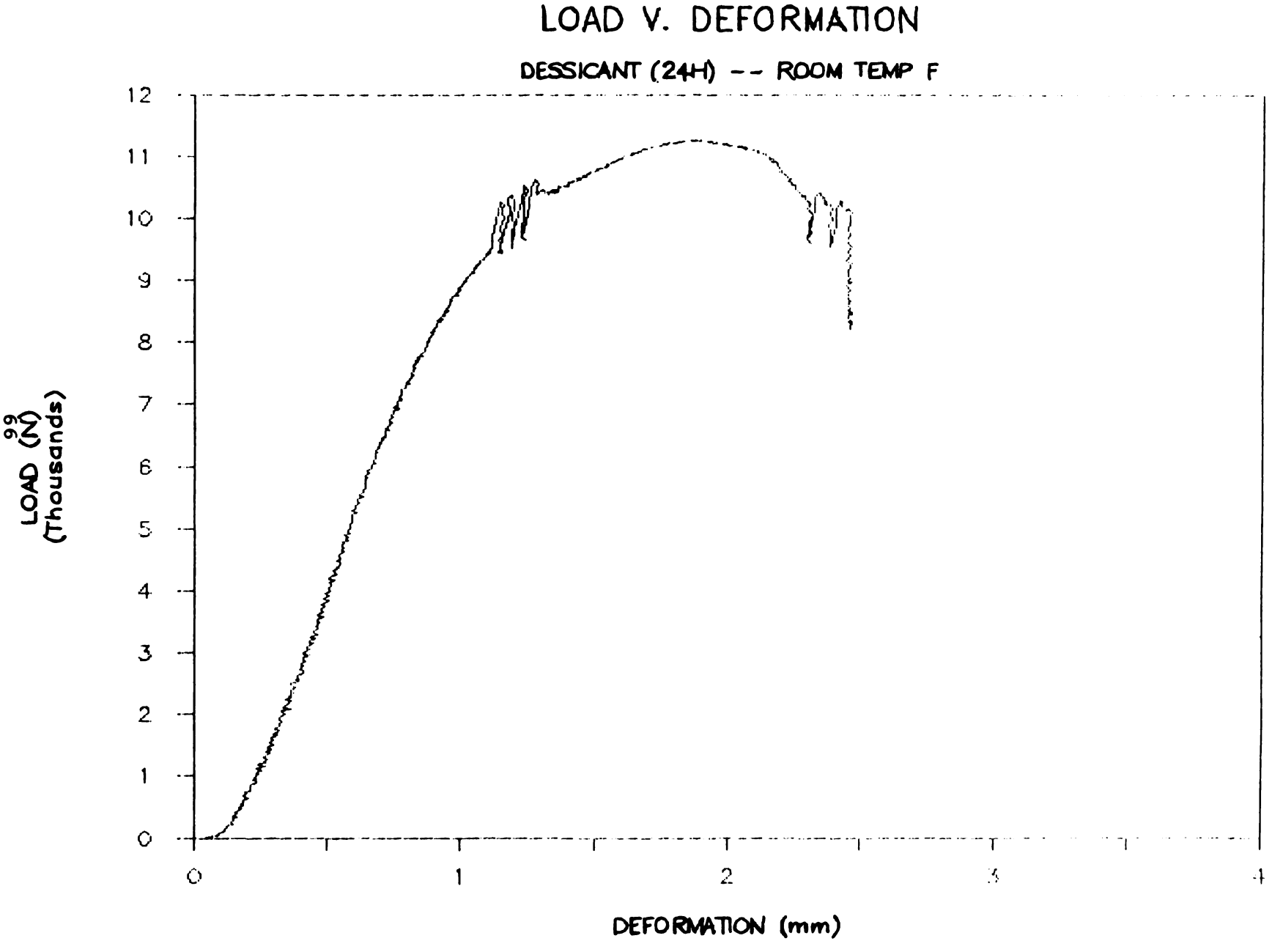
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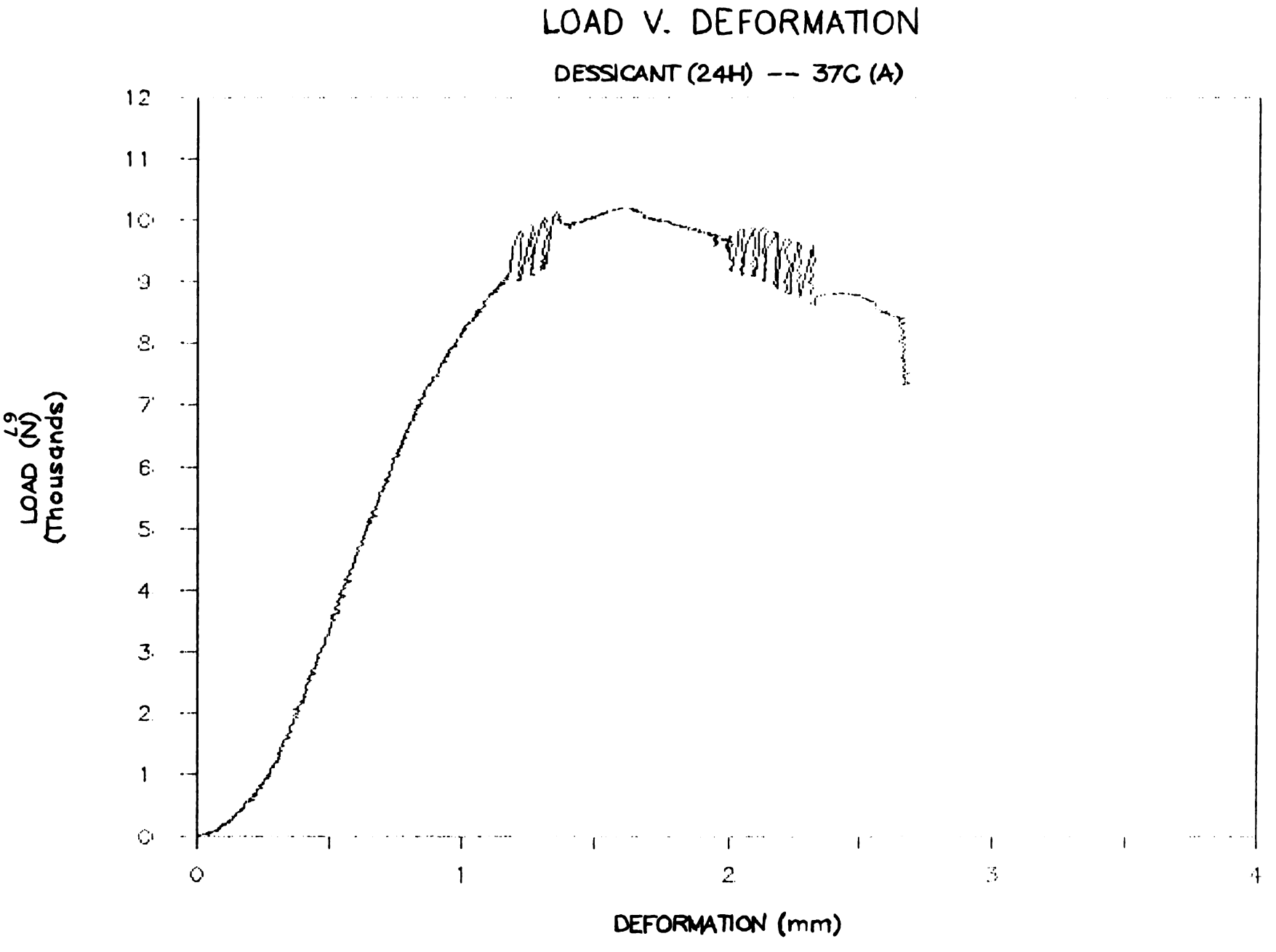
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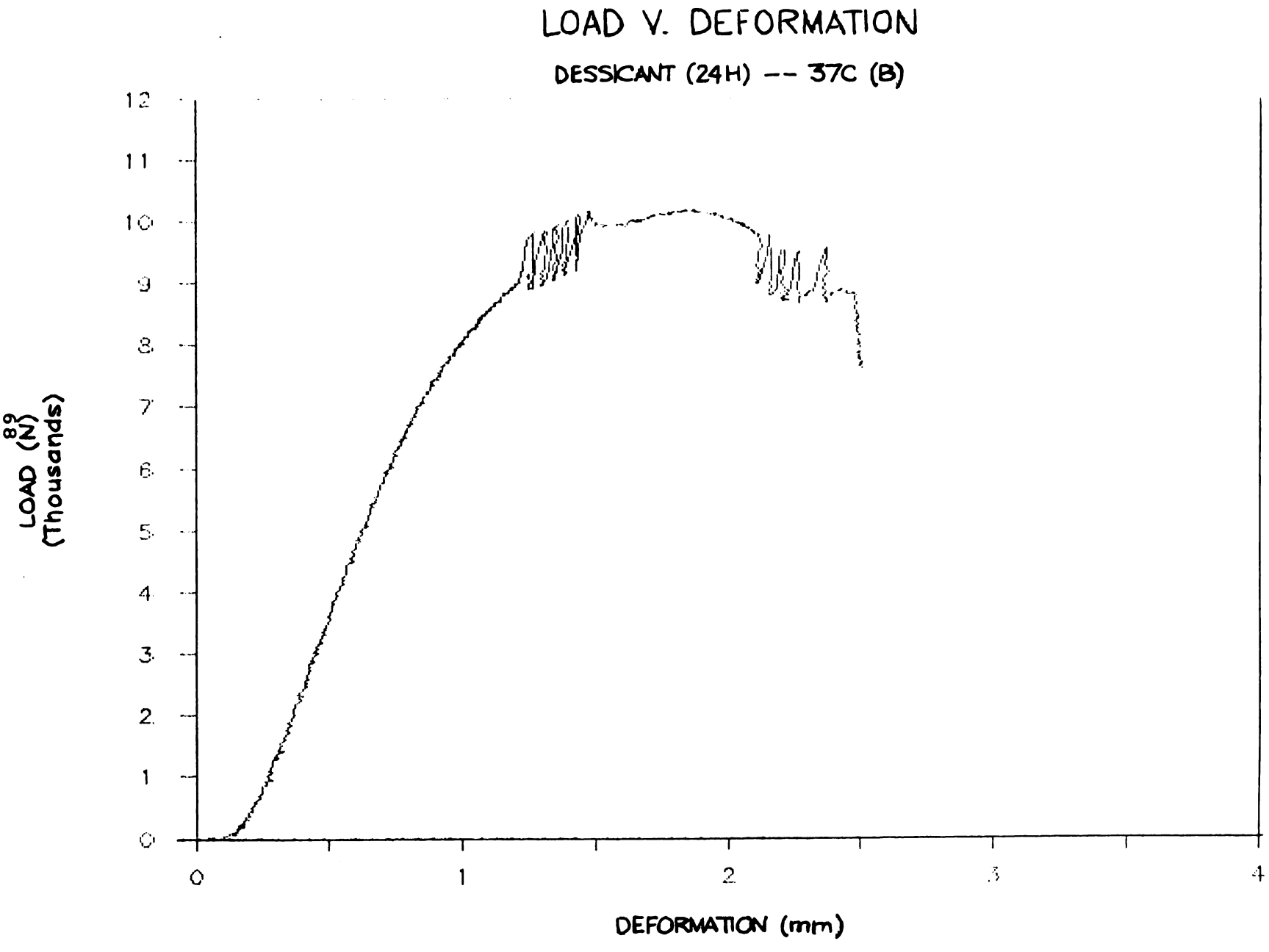
4
DEFORMATION (mm)


LOAD V. DEFORMATION
DESSICANT (24H) -- 37C (B)
LOAD (N) / 89 (Thousands)
12
11
10
9
8
7
6
5
4
3
2
1
0
0
1
2
3
4
DEFORMATION (mm)

LOAD V. DEFORMATION

DESSICANT (24H) -- 37C (C)