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TITLE: Non-Invasive Phosphorus-31 Magnetic Resonance Spectral Characterization of Breast Tissue Anomalies Using Pattern Recognition and Artificial Intelligence

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Final Report on
Non-invasive Phosphorus-31 MR spectral characterization of
***in vivo* breast tissue anomalies using pattern recognition**
and artificial intelligence (AI) techniques

by

Jerry A. Darsey (PI)

I. Introduction:

It is highly desirable to develop a non-invasive spectroscopic and pattern recognition technique that can detect and reliably interpret images or spectral data from small volumes of the breast. Due to the pervasive nature of breast cancer in society today, and the consequent need of a highly accurate, early diagnostic tool, this is a very timely proposal that could have a significant impact on women's health. Patient ROTating Delivery of Excitation Off-resonance (RDEO) MRI data has been obtained from Dr. Diana Lindquist at the University of Arkansas for Medical Sciences. These patients, which flagged suspicious regions in breast tissue, have undergone needle biopsies from these suspect regions for pathological examination. With the patient's permission, Dr. Lindquist obtained P-31 MR scans of the flagged suspect tissue and healthy tissue in the same session. Access to data from 6 patients were obtained and made available for analysis in this study. We proposed to use a combination of pattern recognition techniques, including Artificial Neural Networks (ANN), to develop *in vivo* methods that use breast P-31 MR scans (suspicious and non-suspicious regions) to diagnose potential malignant tissue. The MR scan data will be paired with the known biopsy results to create a supervised training set. Unfortunately two events occurred to prevent us from completing this study[1-3].

First, originally we were to obtain data on 25 patients. However before all 25 patients were scanned, the MRI instrument used in this study was decommissioned for replacement by a more powerful and updated MRI. We successfully completed MRI P-31 scans on only six patients. The transition from old to new MRI required approximately 4 months. Second, the new MRI needed to have a new P-31 MRI probe constructed. Such a task requires expertise in probe design. The expert in this

project with this expertise, Dr. Diana Lindquist, took another job in Cincinnati, Ohio before she was able to develop a new probe for the new MRI.

For the reasons mentioned previously, it is highly desirable to develop a non-invasive spectroscopic and pattern recognition technique that can detect and reliably interpret images or spectral data from small volumes of the breast. Due to the pervasive nature of breast cancer in society today, and the consequent need of a highly accurate, early diagnostic tool, this is a very timely proposal that could have a significant impact on women's health. The results of the brain scan study suggest that breast tumor detection may be possible at a very early stage with this technique given sufficient examples in the training sets [4]. There is a high degree of correlation between the chance of complete eradication, recovery, and survival from cancer and how early it's detected. This is true for breast cancer as it is for all other types of cancer.

II Methods:

A. Subjects:

Seven patients were chosen because they had a suspicious mass found either by mammography or palpation and were scheduled for either surgery or biopsy. They were excluded if they had had a previous core biopsy from the site. The local institutional review board approved this study. A typical MRI instrument containing patient is shown in Figure 1a with corresponding schematic of important components shown in Figure 1b.



Figure 1a: Typical MRI instrument with a patient shown being readied for

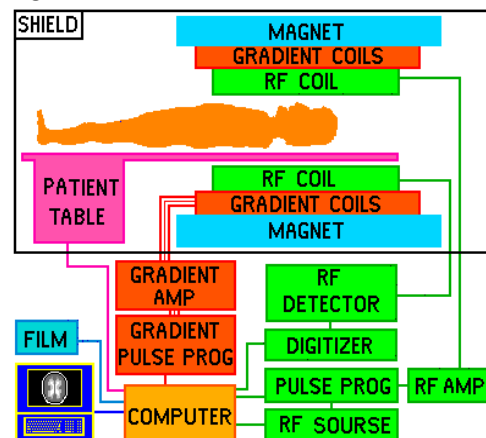


Figure 1b: Schematic of typical MRI instrument used in this project.

MRI scan.

B. MR Data Acquisition

All data were acquired on a 1.5 T General Electric Signa Horizon system (General Electric, Milwaukee, WI, USA) using a home-built solenoid phosphorus coil placed inside a proton transmit/receive bilateral breast coil (MRI Devices, Milwaukee, WI, USA). For these studies, only one breast was examined, so the proton coil was operated as either a right- or left-only coil.

C. Phosphorus-31 coil:

The phosphorus coil consisted of ¼-inch wide copper tape wrapped on an acrylic tube 13.6 cm in diameter. The coil was 9 cm tall from top to bottom. The acrylic tube was fitted with a plastic flange to allow it to hang from the top of the proton breast coil. Variable capacitors were used for tuning and matching the coil, which was done for most of the subjects recruited. A balun was inserted in the coil cable to minimize effects from cable currents. Figure 2 below shows a typical MRI spectra from normal human tissue [1].

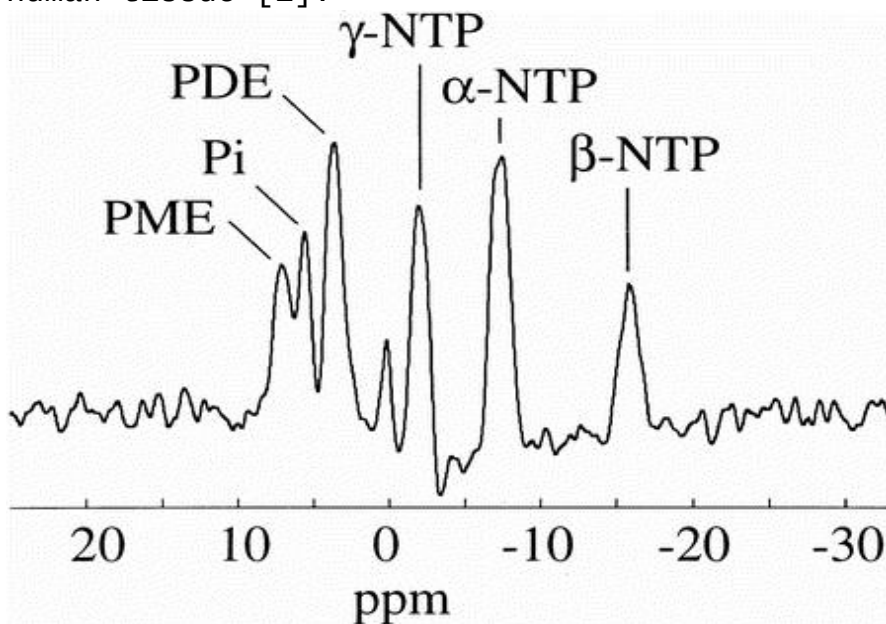


Figure 2. Example of a ^{31}P magnetic resonance spectrum from normal human tissue.

In this ^{31}P magnetic resonance spectrum from normal human tissue we see that the peak area is proportional to amount of metabolite. Peaks labeled on scan: PME, phosphomonoesters (mainly phospholipid precursors, principally phosphocompounds of choline and ethanolamine,

with some contribution from sugar phosphates); P_i , inorganic phosphate (product of ATP hydrolysis); PDE, phosphodiesterases (phospholipid catabolites, mainly glycerophosphocompounds of choline and ethanolamine, with some contribution from cell membranes); and γ -, α -, β -phosphates of nucleotide triphosphates, NTP (high-energy phosphate compounds). By convention, the [β -P] NTP peak is taken to represent ATP. Phosphocreatine peak (not labeled) is at zero parts per million (assumed from muscle contamination). Data are conventionally presented as ratios of related peak areas, comprising phosphoester metabolites (PME/PDE) and energy status (ATP/ P_i) respectively. Alternatively, individual peak areas may be expressed as a function of total visible phosphate (TP). These measures are independent of the volume of liver from which the signals are obtained. Liver intracellular pH (pH_{ic}) was derived from the chemical shift difference between [α -P] NTP, assigned to -7.5 ppm, and P_i , according to the supplied calibration data. ppm, resonance chemical shift in parts per million.

The phosphorus coil (see for example Figures 3 and 4)[2] was centered in the appropriate side of the proton coil and the subject was positioned prone on top of the coils with the breast to be examined hanging freely. The contralateral breast was compressed against the chest to minimize artifacts in the clinical images. The patient was then centered in the magnet (see Figure 1a). Pre- and post-contrast clinical RoDEO images were acquired to localize the lesion (parameters: flip angle: 45 degrees; repetition time 20ms; echo time 5ms; 128x256 matrix; slice thickness 1.4-1.8 mm; 128 slices). A slice containing the lesion was chosen and used as the center point for the spectroscopy exam. The spectroscopy exam used a phase-encoded pulse acquire technique (parameters: 25 degree flip angle, repetition time 300ms, 6 x 6 matrix, 512 complex points, 2000 Hz spectral width, 75 NEX, 200 mm FOV, and 30 mm slice thickness). Each spectral data set required about 30 minutes to acquire. To assess the reproducibility of the technique, spectra were acquired on three separate days from one volunteer. For all other subjects, spectra were acquired once.

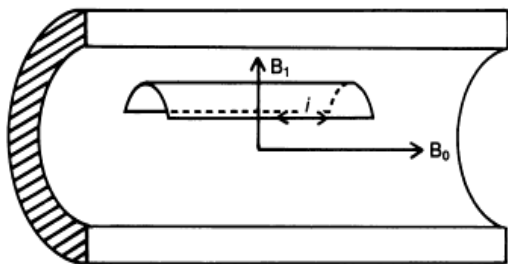


Figure 3. A saddle-shaped radio frequency (RF) coil inside a solenoid magnet. B_0 =the direction of the magnetic field of the solenoidal magnet, B_1 =the direction of the magnetic field produced by current flow, i , in the RF coil.

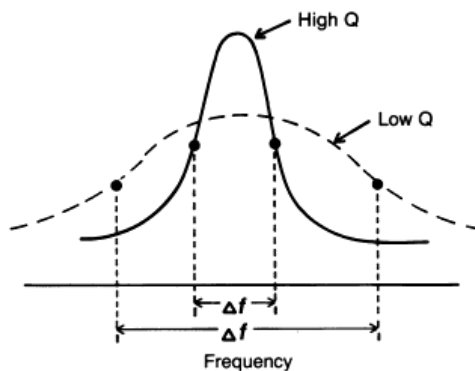


Figure 4. Dependence of bandwidth, Δf , of coil on value of Q .

Data were transferred to an off-line workstation (SGI O₂ system) for processing and analysis. The data were processed using SA/GE (Spectral analysis software, General Electric, Milwaukee, WI, USA). All data were given 10 Hz of exponential line-broadening prior to Fourier transformation. The data were phased automatically, with some manual phasing of individual spectra if needed. The phased spectra were overlaid on the central image from the clinical exam for display [5-7].

III Key Research Accomplishments in first year:

- Ran MRIs on six patients using RoDEO enhancements to pinpoint potential breast tissue anomalies.
- Ran 36 voxels of data for P-31 spectra on all 6 patients.
- Thirty-six, 180 cm³ voxels were obtained and the corresponding P-31 spectra were obtained for each MRI scan of each patient.
- The 36 spectra per patient were examined to locate the peaks from phosphomonoesters, phosphodiesteres, phosphocreatine, inorganic phosphate, and the ATP peaks.
- Analysis was attempted with artificial neural network software. The signal-to-noise ratio was very low and made difficult the unambiguous determination of either the location or intensity of any of peaks [6,7].

IV. Reportable Outcomes in first year:

The following are examples of both the MRI images of a breast (Figure 5a and Figure 6a) and the corresponding P-31 spectra (Figure 5b and Figure 6b) of the lesion which was targeted. The "aqua" spectra seen on the breast image is located in the area of the voxel where the P-31 spectra was obtained. Spectra were obtained for both normal (benign) tissue and potentially malignant tissue.

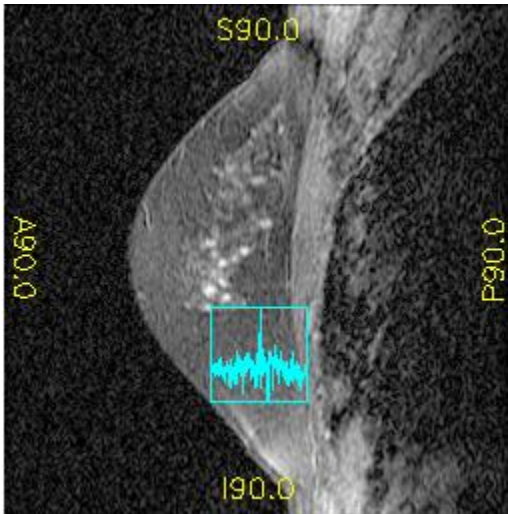


Figure 5a: Example of MRI image of Patient 1(breast normal tissue)

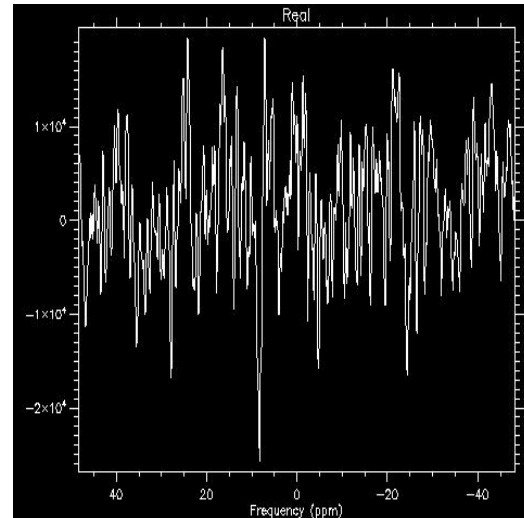


Figure 5b: P-31 spectra of breast on left for Patient 1

The following figures (Figure 6a and 6b) show the MRI image and corresponding P-31 spectra for a patient with a diagnosed malignant tumor.

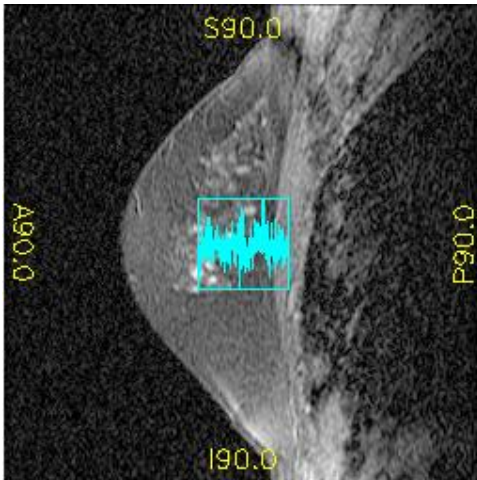


Figure 6a: MRI image of breast for Patient 2 (suspected malignant area)

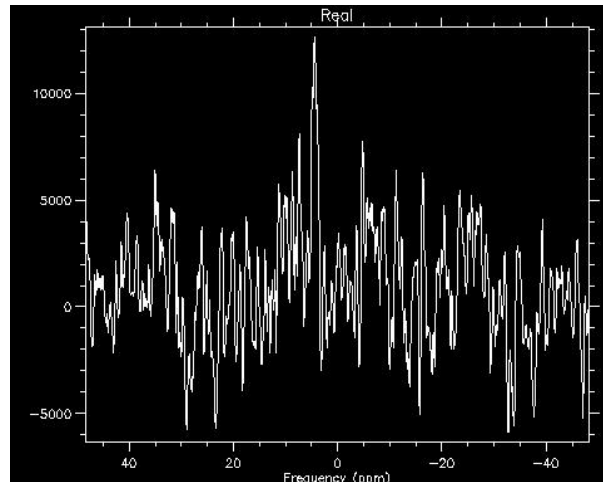


Figure 6b: P-31 spectra of breast on left for Patient 2.

The raw data from the phosphorus scan, as previously stated, was transferred to an SGI O₂ workstation for offline processing using the GE Spectral Analysis (SA/GE) package. This data was processed to achieve as good a resolution as possible and the signal to noise ratios minimized, which required zero-filling and apodizing the raw data prior to Fourier transformation. The precise processing parameters will be determined from the first data set and will be used consistently throughout this project. Initial processing parameters will be zero-filling once with 10 Hz exponential line broadening applied.

Work performed on project with No-cost Extension in 2nd Year:

Experimental:

We initially attempted to analyze samples of breast tissue for P-31 signal. We took samples of tissue and placed it into a test tube. We sonicated the samples for 2, 4, and 8 hours. The samples were placed in three solvents; water, methanol, and ethanol. After each sonication, we pored off the supernatant and ran an NMR on the resulting solution. The University has a 200 MHz FT NMR with a multi-nuclei probe. The samples had no detectable P-31 signal.

Patient Data Analysis:

We were able to make limited analysis on the data on the 6 patients we were able to obtain P-31 spectra on. Although this data was very, very noisy, and after numerous trial-and-error, we managed to obtain a tentative correlation plot which indicated that the neural network was able to "see through the noise" and produce some very preliminary results. Figure 7 below shows a plot of the analysis of the raw data of the six patients with only one patient confirmed with a malignant tumor. However, when the data was analyzed, there seemed to be at least one other patient with a potential malignant tumor. This is the data point pointed to by the arrow. However, the correlation was not strong and it did not show up in all of our artificial network trainings. Basically, along the "predicted" axis of this plot, a number close to zero indicates non-cancerous and a number close to 1 indicated a cancerous tumor. Note that the numbers close to zero ranged between about -0.3 and +0.4. The number for a "positive" result was +0.78 and 1.42 on the predicted axis, although the data was trained between 0.05 and 0.95. We used a leave-one-out method to propagate our data, that is,

we trained on 5 data points and propagated the sixth patient data point. We took a positive to be any number greater than 0.5 when propagated. We re-plotted the data now with the assumption that the data point pointed to by the arrow, was malignant. Therefore the second point at about 0.9,0.78 (patient 6) was considered malignant. We unfortunately do not have biopsy data to confirm that the tissue analyzed for patient 6 is malignant.

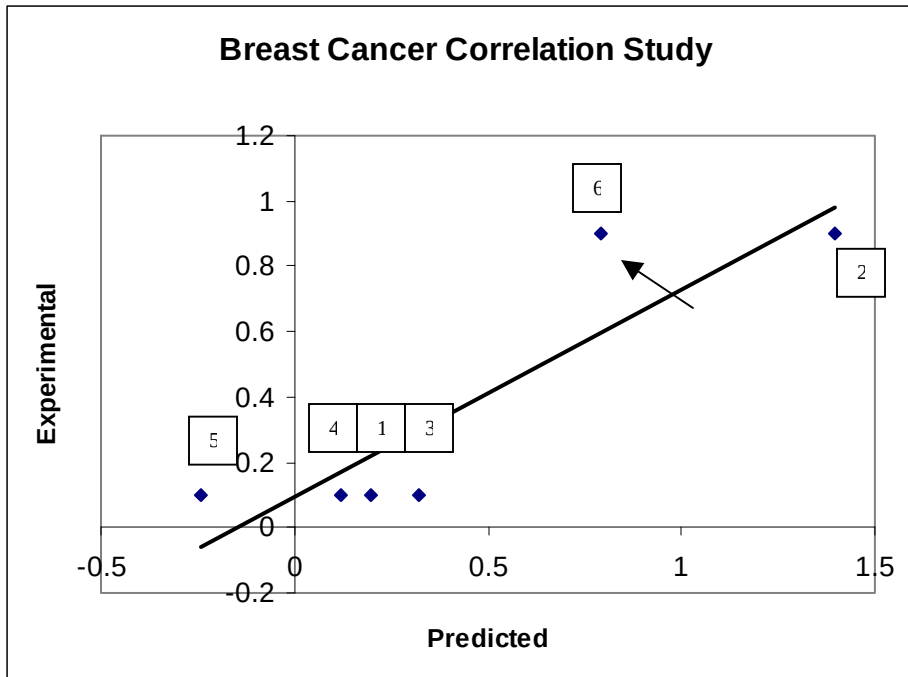


Figure 7: Correlation plot of the experimental results vs. predicted results from the artificial neural network for 6 patients. The arrow indicates a possible malignant tumor in patient 6. The numbers indicate patient number.

V. Summary of Project:

With breast cancer being the number one cancer in woman with over 200,000 diagnosed this year, and more than 1.6 million women a survivor of this cancer, we strongly believe that the procedure outlined in this research proposal has the potential to provide a much earlier diagnosis which should reduce the need of biopsies, and,

potentially provide a much higher cure rate due to this earlier detection and diagnosis [11,12].

Due to the very limited number of patients (6), it was not possible to perform extensive artificial neural network analysis. We originally wanted to study at least 25 patients, of which at least half, or approximately 10 were to be diagnosed with a malignant tumor verified using a biopsy. However, we were only able to recruit 6 patients with only one patient (patient 2) having a confirmed malignant breast tumor. The biggest problem was that my major Co-PI, Dr. Diana Lindquist, is no longer available for this project. She has accepted as of May, 2006 another position in Cleveland, Ohio. Therefore we will not be able to perform any additional MRI scans with the accompanying P-31 spectra for analysis. Attempts were made to obtain some tissue samples, some containing a malignant tumor and some normal tissue. We were able to secure some tissue for testing purposes, however, we were never able to develop a procedure which allowed us to perform P-31 NMR on these samples. However, I have a new student in my group who wishes to continue this project and he will be working on developing some procedures to allow us to obtain P-31 NMR spectra on malignant and non-malignant breast tissue.

VI. Future Research:

A major problem in continuing this project is that my major collaborators on this project no longer are in Arkansas and are not available for continued research. However, I have made a new contact at the University of Arkansas for Medical Sciences [UAMS] (Dr. Larry J. Suva), and have a new PhD student majoring in our bioinformatics program who wishes to continue this project. He will be obtaining new samples of cancer and non-cancer breast tissue for analysis using NMR. He will be looking at both P-31 as well as the gadolinium isotope, an isotope used in the RODIO studies. These studies should lead to improved prediction of the non-invasive malignant and non-malignant tumors in breast tissue. This work will be conducted without additional funding for the previous breast cancer funding.

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VII Appendix:

Table 1. The following data is an example of MRI P-31 spectral data obtained from one run of one voxel from one patient. This is only one data set of 36 per patient.

-48.3372	-910.782	-3245.02	-48.3372	-910.782	-3245.02	-48.3372	-910.782	-3245.02
-48.2428	-1690.84	-2147.08	-48.2428	-1690.84	-2147.08	-48.2428	-1690.84	-2147.08
-48.1484	-1914.17	-1049.76	-48.1484	-1914.17	-1049.76	-48.1484	-1914.17	-1049.76
-48.054	-1688.97	173.7177	-48.054	-1688.97	173.7177	-48.054	-1688.97	173.7177
-47.9596	-622.148	1054.866	-47.9596	-622.148	1054.866	-47.9596	-622.148	1054.866
-47.8652	532.5189	938.0002	-47.8652	532.5189	938.0002	-47.8652	532.5189	938.0002
-47.7707	1215.161	453.6369	-47.7707	1215.161	453.6369	-47.7707	1215.161	453.6369
-47.6763	1648.259	-372.932	-47.6763	1648.259	-372.932	-47.6763	1648.259	-372.932
-47.5819	1159.117	-1339.67	-47.5819	1159.117	-1339.67	-47.5819	1159.117	-1339.67
-47.4875	131.9281	-1267.76	-47.4875	131.9281	-1267.76	-47.4875	131.9281	-1267.76
-47.3931	-48.5061	-412.905	-47.3931	-48.5061	-412.905	-47.3931	-48.5061	-412.905
-47.2987	604.1929	-197.056	-47.2987	604.1929	-197.056	-47.2987	604.1929	-197.056
-47.2043	710.0126	-685.19	-47.2043	710.0126	-685.19	-47.2043	710.0126	-685.19
-47.1099	334.7101	-699.416	-47.1099	334.7101	-699.416	-47.1099	334.7101	-699.416
-47.0155	234.1037	-402.606	-47.0155	234.1037	-402.606	-47.0155	234.1037	-402.606
-46.9211	401.9159	-60.7045	-46.9211	401.9159	-60.7045	-46.9211	401.9159	-60.7045
-46.8267	881.0281	20.64682	-46.8267	881.0281	20.64682	-46.8267	881.0281	20.64682
-46.7323	1203.557	-233.799	-46.7323	1203.557	-233.799	-46.7323	1203.557	-233.799
-46.6378	1443.263	-491.816	-46.6378	1443.263	-491.816	-46.6378	1443.263	-491.816
-46.5434	1641.428	-1032.7	-46.5434	1641.428	-1032.7	-46.5434	1641.428	-1032.7
-46.449	1343.275	-1658.83	-46.449	1343.275	-1658.83	-46.449	1343.275	-1658.83
-46.3546	899.7252	-1890.39	-46.3546	899.7252	-1890.39	-46.3546	899.7252	-1890.39
-46.2602	545.8783	-2253.32	-46.2602	545.8783	-2253.32	-46.2602	545.8783	-2253.32
-46.1658	-512.042	-2543.14	-46.1658	-512.042	-2543.14	-46.1658	-512.042	-2543.14
-46.0714	-1746.02	-1648.69	-46.0714	-1746.02	-1648.69	-46.0714	-1746.02	-1648.69
-45.977	-1805.84	-45.4079	-45.977	-1805.84	-45.4079	-45.977	-1805.84	-45.4079
-45.8826	-832.514	929.9805	-45.8826	-832.514	929.9805	-45.8826	-832.514	929.9805
-45.7882	242.5123	1167.244	-45.7882	242.5123	1167.244	-45.7882	242.5123	1167.244
-45.6938	1389.665	865.2434	-45.6938	1389.665	865.2434	-45.6938	1389.665	865.2434
-45.5994	2100.71	-268.273	-45.5994	2100.71	-268.273	-45.5994	2100.71	-268.273
-45.5049	1782.054	-1476.76	-45.5049	1782.054	-1476.76	-45.5049	1782.054	-1476.76
-45.4105	839.2883	-2021.62	-45.4105	839.2883	-2021.62	-45.4105	839.2883	-2021.62
-45.3161	57.37751	-1651.71	-45.3161	57.37751	-1651.71	-45.3161	57.37751	-1651.71
-45.2217	194.5479	-1175.96	-45.2217	194.5479	-1175.96	-45.2217	194.5479	-1175.96
-45.1273	488.801	-1497.75	-45.1273	488.801	-1497.75	-45.1273	488.801	-1497.75
-45.0329	98.8756	-2072.64	-45.0329	98.8756	-2072.64	-45.0329	98.8756	-2072.64
-44.9385	-791.473	-2049.57	-44.9385	-791.473	-2049.57	-44.9385	-791.473	-2049.57
-44.8441	-1161.86	-1294.43	-44.8441	-1161.86	-1294.43	-44.8441	-1161.86	-1294.43
-44.7497	-755.977	-988.529	-44.7497	-755.977	-988.529	-44.7497	-755.977	-988.529
-44.6553	-700.569	-1386.64	-44.6553	-700.569	-1386.64	-44.6553	-700.569	-1386.64
-44.5609	-1350.74	-1646.55	-44.5609	-1350.74	-1646.55	-44.5609	-1350.74	-1646.55
-44.4665	-2206.08	-1110.13	-44.4665	-2206.08	-1110.13	-44.4665	-2206.08	-1110.13
-44.372	-2266.56	-37.3928	-44.372	-2266.56	-37.3928	-44.372	-2266.56	-37.3928
-44.2776	-1668.78	436.3974	-44.2776	-1668.78	436.3974	-44.2776	-1668.78	436.3974
-44.1832	-1412.6	394.9462	-44.1832	-1412.6	394.9462	-44.1832	-1412.6	394.9462
-44.0888	-1379.66	561.672	-44.0888	-1379.66	561.672	-44.0888	-1379.66	561.672
-43.9944	-1136.29	649.5616	-43.9944	-1136.29	649.5616	-43.9944	-1136.29	649.5616

Table 1. (continued)

-43.8056	-1591.39	852.8599	-43.8056	-1591.39	852.8599	-43.8056	-1591.39	852.8599
-43.7112	-1388.02	1590.894	-43.7112	-1388.02	1590.894	-43.7112	-1388.02	1590.894
-43.6168	-634.574	1846.226	-43.6168	-634.574	1846.226	-43.6168	-634.574	1846.226
-43.5224	-182.489	1410.253	-43.5224	-182.489	1410.253	-43.5224	-182.489	1410.253
-43.428	-488.897	1076.503	-43.428	-488.897	1076.503	-43.428	-488.897	1076.503
-43.3335	-864.559	1542.665	-43.3335	-864.559	1542.665	-43.3335	-864.559	1542.665
-43.2391	-409.926	2175.018	-43.2391	-409.926	2175.018	-43.2391	-409.926	2175.018
-43.1447	157.087	2021.55	-43.1447	157.087	2021.55	-43.1447	157.087	2021.55
-43.0503	53.60254	1965.013	-43.0503	53.60254	1965.013	-43.0503	53.60254	1965.013
-42.9559	236.5543	2521.127	-42.9559	236.5543	2521.127	-42.9559	236.5543	2521.127
-42.8615	1067.008	2861.864	-42.8615	1067.008	2861.864	-42.8615	1067.008	2861.864
-42.7671	2035.068	2654.501	-42.7671	2035.068	2654.501	-42.7671	2035.068	2654.501
-42.6727	2928.347	1971.809	-42.6727	2928.347	1971.809	-42.6727	2928.347	1971.809
-42.5783	3358.361	679.5933	-42.5783	3358.361	679.5933	-42.5783	3358.361	679.5933
-42.4839	2812.034	-499.876	-42.4839	2812.034	-499.876	-42.4839	2812.034	-499.876
-42.3895	2078.374	-987.662	-42.3895	2078.374	-987.662	-42.3895	2078.374	-987.662
-42.2951	1373.647	-1403.6	-42.2951	1373.647	-1403.6	-42.2951	1373.647	-1403.6
-42.2006	286.4179	-1424.81	-42.2006	286.4179	-1424.81	-42.2006	286.4179	-1424.81
-42.1062	-555.958	-752.619	-42.1062	-555.958	-752.619	-42.1062	-555.958	-752.619
-42.0118	-935.479	172.0492	-42.0118	-935.479	172.0492	-42.0118	-935.479	172.0492
-41.9174	-711.475	1285.723	-41.9174	-711.475	1285.723	-41.9174	-711.475	1285.723
-41.823	243.7521	1887.929	-41.823	243.7521	1887.929	-41.823	243.7521	1887.929
-41.7286	1118.031	1723.481	-41.7286	1118.031	1723.481	-41.7286	1118.031	1723.481
-41.6342	1583.468	1243.045	-41.6342	1583.468	1243.045	-41.6342	1583.468	1243.045
-41.5398	1689.699	854.5495	-41.5398	1689.699	854.5495	-41.5398	1689.699	854.5495
-41.4454	1887.802	530.306	-41.4454	1887.802	530.306	-41.4454	1887.802	530.306
-41.351	1869.176	-115.247	-41.351	1869.176	-115.247	-41.351	1869.176	-115.247
-41.2566	1320.6	-613.754	-41.2566	1320.6	-613.754	-41.2566	1320.6	-613.754
-41.1621	548.4608	-553.633	-41.1621	548.4608	-553.633	-41.1621	548.4608	-553.633
-41.0677	169.6563	27.68352	-41.0677	169.6563	27.68352	-41.0677	169.6563	27.68352
-40.9733	287.343	482.1457	-40.9733	287.343	482.1457	-40.9733	287.343	482.1457
-40.8789	465.1859	643.5623	-40.8789	465.1859	643.5623	-40.8789	465.1859	643.5623
-40.7845	436.7585	800.9824	-40.7845	436.7585	800.9824	-40.7845	436.7585	800.9824
-40.6901	655.709	1258.421	-40.6901	655.709	1258.421	-40.6901	655.709	1258.421
-40.5957	1265.602	1291.614	-40.5957	1265.602	1291.614	-40.5957	1265.602	1291.614
-40.5013	1546.083	990.8132	-40.5013	1546.083	990.8132	-40.5013	1546.083	990.8132
-40.4069	1661.777	774.5599	-40.4069	1661.777	774.5599	-40.4069	1661.777	774.5599
-40.3125	1750.604	542.1177	-40.3125	1750.604	542.1177	-40.3125	1750.604	542.1177
-40.2181	1698.236	223.1239	-40.2181	1698.236	223.1239	-40.2181	1698.236	223.1239
-40.1237	1400.869	47.88004	-40.1237	1400.869	47.88004	-40.1237	1400.869	47.88004
-40.0292	1095.401	106.7472	-40.0292	1095.401	106.7472	-40.0292	1095.401	106.7472
-39.9348	785.3507	344.7289	-39.9348	785.3507	344.7289	-39.9348	785.3507	344.7289
-39.8404	581.1136	966.6189	-39.8404	581.1136	966.6189	-39.8404	581.1136	966.6189
-39.746	1094.592	1895.979	-39.746	1094.592	1895.979	-39.746	1094.592	1895.979
-39.6516	2400.454	2055.838	-39.6516	2400.454	2055.838	-39.6516	2400.454	2055.838
-39.5572	3264.755	1286.623	-39.5572	3264.755	1286.623	-39.5572	3264.755	1286.623
-39.4628	3576.869	486.9435	-39.4628	3576.869	486.9435	-39.4628	3576.869	486.9435
-39.3684	3654.662	-417.049	-39.3684	3654.662	-417.049	-39.3684	3654.662	-417.049
-39.274	3095.014	-1304.43	-39.274	3095.014	-1304.43	-39.274	3095.014	-1304.43
-39.1796	2165.288	-1392.04	-39.1796	2165.288	-1392.04	-39.1796	2165.288	-1392.04

Table 1. (continued)

-39.0852	1868.401	-851.317	-39.0852	1868.401	-851.317	-39.0852	1868.401	-851.317
-38.9907	2328.221	-664.094	-38.9907	2328.221	-664.094	-38.9907	2328.221	-664.094
-38.8963	2662.348	-1368.09	-38.8963	2662.348	-1368.09	-38.8963	2662.348	-1368.09
-38.8019	2035.069	-2134.88	-38.8019	2035.069	-2134.88	-38.8019	2035.069	-2134.88
-38.7075	1126.071	-2161.85	-38.7075	1126.071	-2161.85	-38.7075	1126.071	-2161.85
-38.6131	427.0704	-1735.19	-38.6131	427.0704	-1735.19	-38.6131	427.0704	-1735.19
-38.5187	117.3701	-998.099	-38.5187	117.3701	-998.099	-38.5187	117.3701	-998.099
-38.4243	270.3219	-340.054	-38.4243	270.3219	-340.054	-38.4243	270.3219	-340.054
-38.3299	605.017	152.7145	-38.3299	605.017	152.7145	-38.3299	605.017	152.7145
-38.2355	1298.704	543.0816	-38.2355	1298.704	543.0816	-38.2355	1298.704	543.0816
-38.1411	2218.775	161.337	-38.1411	2218.775	161.337	-38.1411	2218.775	161.337
-38.0467	2298.62	-648.663	-38.0467	2298.62	-648.663	-38.0467	2298.62	-648.663
-37.9523	2065.599	-883.108	-37.9523	2065.599	-883.108	-37.9523	2065.599	-883.108
-37.8578	2018.563	-1031.5	-37.8578	2018.563	-1031.5	-37.8578	2018.563	-1031.5
-37.7634	1994.053	-1019.03	-37.7634	1994.053	-1019.03	-37.7634	1994.053	-1019.03
-37.669	2434.039	-1078.69	-37.669	2434.039	-1078.69	-37.669	2434.039	-1078.69
-37.5746	2926.522	-1836.27	-37.5746	2926.522	-1836.27	-37.5746	2926.522	-1836.27
-37.4802	2797.235	-3020.37	-37.4802	2797.235	-3020.37	-37.4802	2797.235	-3020.37
-37.3858	1955.65	-4154.11	-37.3858	1955.65	-4154.11	-37.3858	1955.65	-4154.11
-37.2914	404.4081	-4773.69	-37.2914	404.4081	-4773.69	-37.2914	404.4081	-4773.69
-37.197	-1253.91	-4391.2	-37.197	-1253.91	-4391.2	-37.197	-1253.91	-4391.2
-37.1026	-2350.22	-3401.23	-37.1026	-2350.22	-3401.23	-37.1026	-2350.22	-3401.23
-34.7424	3228.471	-2040.56	-34.7424	3228.471	-2040.56	-34.7424	3228.471	-2040.56
-34.648	3100.886	-3279.93	-34.648	3100.886	-3279.93	-34.648	3100.886	-3279.93
-34.5535	1600.654	-4325.02	-34.5535	1600.654	-4325.02	-34.5535	1600.654	-4325.02
-34.4591	-486.409	-3841.55	-34.4591	-486.409	-3841.55	-34.4591	-486.409	-3841.55
-34.3647	-1738.76	-1897.63	-34.3647	-1738.76	-1897.63	-34.3647	-1738.76	-1897.63
-34.2703	-1260.44	472.7027	-34.2703	-1260.44	472.7027	-34.2703	-1260.44	472.7027
-34.1759	703.5732	1766.938	-34.1759	703.5732	1766.938	-34.1759	703.5732	1766.938
-34.0815	2688.591	1443.014	-34.0815	2688.591	1443.014	-34.0815	2688.591	1443.014
-33.9871	3933.663	426.366	-33.9871	3933.663	426.366	-33.9871	3933.663	426.366
-33.8927	4650.686	-1056.43	-33.8927	4650.686	-1056.43	-33.8927	4650.686	-1056.43
-33.7983	4258.882	-2612.09	-33.7983	4258.882	-2612.09	-33.7983	4258.882	-2612.09
-33.7039	3496.437	-3301.98	-33.7039	3496.437	-3301.98	-33.7039	3496.437	-3301.98
-33.6095	2949.12	-3946.55	-33.6095	2949.12	-3946.55	-33.6095	2949.12	-3946.55
-33.5151	1877.297	-4492.99	-33.5151	1877.297	-4492.99	-33.5151	1877.297	-4492.99
-33.4206	579.0143	-4356.7	-33.4206	579.0143	-4356.7	-33.4206	579.0143	-4356.7
-33.3262	-573.111	-3364.94	-33.3262	-573.111	-3364.94	-33.3262	-573.111	-3364.94
-33.2318	-498.53	-1619.73	-33.2318	-498.53	-1619.73	-33.2318	-498.53	-1619.73
-33.1374	984.8907	-942.968	-33.1374	984.8907	-942.968	-33.1374	984.8907	-942.968
-33.043	1890.062	-1726.66	-33.043	1890.062	-1726.66	-33.043	1890.062	-1726.66
-32.9486	1781.755	-2332.74	-32.9486	1781.755	-2332.74	-32.9486	1781.755	-2332.74
-32.8542	1768.243	-2494.29	-32.8542	1768.243	-2494.29	-32.8542	1768.243	-2494.29
-32.7598	1813.553	-2827.02	-32.7598	1813.553	-2827.02	-32.7598	1813.553	-2827.02
-32.6654	1756.955	-3052.58	-32.6654	1756.955	-3052.58	-32.6654	1756.955	-3052.58