Supplemental Materials

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Group	Measurements	MRI Sequences	Comments
1 (n=6; 4 diabetes, 2 controls)	T2, T2*, pancreatic volume, lymph nodes	Dual echo GE Dual echo SE	Significant residual intravascular probe at 24 hours. Dual echo sequences without adequate granularity
2 (n=9; 9 diabetes)	T2*, pancreatic volume, lymph nodes	6 echo GE Dual echo SE 3D GE Dual echo in/out of phase	Multiecho sequences implemented. Delayed measurements at 48 and 72 hours compared (48 hours selected).
3 (n=22; 10 diabetes, 12 controls)	T2, T2*, pancreatic volume, lymph nodes	6 echo GE 3 echo SE 3D VIBE Dual echo in/out of phase	Delayed measurements made at 48 hours. T2* measurements limited by susceptibility artifacts

Table S1. Development of imaging protocol through derivation and validation groups. Study groups 1 and 2 were used for protocol development with the readers aware of the study subject's disease status. Group 3 was analyzed with a masked data set. Many of the group 3 T2* sequences had significant susceptibility artifact obscuring the region of the pancreas and were deemed uninterpretable even after unmasking. These T2* sequences were therefore excluded from the final analysis. GE gradient-echo; SE spin-echo.

								HLA Alleles				AutoAbs		
ID	Sex (M/F)	Age (yr)	BMI (kg/m^2)	BSA (m^2)	HbA1c (%)	TTD (days)	TDD (U/kg)	DRB1-Allele1	DQB1-Allele1	DRB1-Allele2	DQB1-Allele2	CIAA (0-39)	GAD (0-0.099)	IA2 (0-0.099)
P-1	F	23.1	19.8	1.54	5.9	147	0.48	3	0201	4	0302	296	0	0.23
P-2	M	19.5	21.9	1.88	7.1	154	0.17	7	0202	4	0302	1170	0.57	8.37
P-3	M	37.4	23.8	1.97	11.6	115	0.13	1	NA	4	0302	21	0.14	0.03
P-4	M	20.8	22.1	1.83	10.2	30	0.78	4	0302	13	0602	70	0.01	0
P-5	M	19.0	23.8	1.90	10.0	51	0.61	3	0201	13	NA	70	0.14	0
P-6	M	65.4	25.2	2.10	10.5	41	0.37	11	0301	12	0301	100	1.12	0.07
P-7	M	42.2	23.7	1.96	6.7	156	0	3	0201	7	0202	8	0.96	0.02
P-8	M	25.7	26.2	1.94	10.0	54	0.31	8	0301	4	0302	0	0.58	8.14
P-9	M	21.1	22.7	1.91	9.5	96	0.58	3	0201	4	0302	213	0.09	12.21
P-10	F	18.2	20.7	1.77	6.7	176	0.30	1	0301	11	0301	627	1.08	7.35
C-1	M	23.8	21.3	1.60	5.5	NA	0	2	NA	13	NA	28	0.04	0
C-2	M	26.1	28.3	2.11	5.0	NA	0	1	NA	11	0301	8	0.03	0
C-3	F	25.3	22.5	1.67	5.2	NA	0	3	0201	7	0202	2	0.02	0
C-4	M	20.1	24.3	1.92	5.2	NA	0	3	0201	11	0301	0	0	0
C-5	M	31.7	22.2	1.83	5.2	NA	0	11	0301	2	0602	0	0	0
C-6	F	46.8	19.6	1.65	5.3	NA	0	4	0301	4	0302	17	0	0.05
C-7	M	47.6	26.4	1.89	5.1	NA	0	2	NA	3	0201	37	0	0.02
C-8	M	23.0	22.9	1.98	5.5	NA	0	7	0202	2	0602	ND	ND	ND
C-9	F	44.0	22.1	1.78	5.6	NA	0	11	0301	4	0302	19	0	0
C-10	M	35.9	21.6	1.84	5.1	NA	0	9	0202	2	0602	19	0.01	0
C-11	M	22.1	23.7	2.01	5.1	NA	0	13	0301	2	0602	7	0	0
C-12	F	21.2	21.6	1.60	5.3	NA	0	2	NA	13	NA	0	0.04	ND

Table S2. Detailed characteristics of validation group participants. Patients recently diagnosed with T1D are labeled P1-10, normal controls are C1-12. All testing was performed as described in the Materials and Methods and Supplemental Methods. BMI, body mass index; BSA, body surface area; HbA1c, hemoglobin A1c; TTD, total time from diagnosis to imaging; TDD, total daily dose of insulin.

Measurement	T1D	Controls	P-value	ROC AUC
Pancreas Volume (mL)	45.6 ± 12.2	64.3 ± 21.8	0.026	0.79
PVI (mL/m^2)	24.1 ± 5.7	35.0 ± 11.5	0.007*	0.85
Delta T2 Pancreas (msec)	14.1 ± 4.7	7.1 ± 4.9	0.005	0.85
Delta T2 Muscle (msec)	1.28 ± 0.78	1.23 ± 0.90	0.784	0.53
Composite Index	59.7 ± 20.2	22.5 ± 17.5	0.0005	0.91

Table S3. Summary of results. *P-value calculated using Mann-Whitney U test as Shapiro-Wilk normality test was failed; all other comparisons performed with two-tailed t-test with Welch's correction for unequal variance. PVI, Pancreas Volume Index is calculated by dividing pancreas volume by body-surface area. Composite Index is calculated using the formula 100 x $\Delta T2_{pancreas}$/PVI. Values presented are mean ± SD. The Composite Index with a cutoff of 40 has a sensitivity of 89% and specificity of 91%.

Figure. S1. Lack of correlation between pancreas volume index and change in T2 within the pancreas. There is no correlation between PVI and delta T2 for patients (circles) and/or controls (squares).

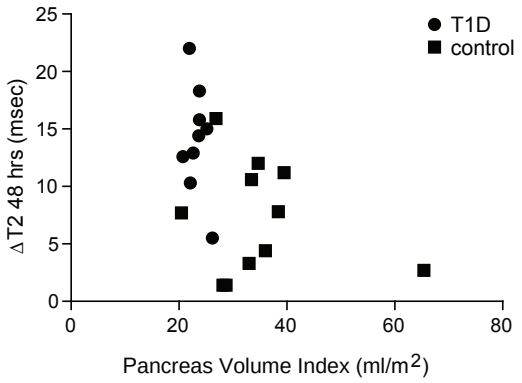

Fig. S1.
Lack of correlation between pancreas volume index and change in T2 within the pancreas.

Supplemental Methods

Study participants. The validation group consisted of 10 individuals recently diagnosed with T1D and 12 normal controls. One control subject and one individual with T1D had possible reactions related to ferumoxtran-10 administration, a rash and a cough respectively. The control subject did not complete ferumoxtran-10 infusion as the rash developed during infusion, and was therefore excluded from all imaging analyses. The individual with T1D noted a cough after completion of the post-injection images. Since ferumoxtran-10-related reactions may involve histamine release and changes in vascular permeability, any individual with a possible contrast reaction was excluded from probe-accumulation analysis. Using this a priori criterion, the individual with T1D and a possible reaction was excluded from the probe-accumulation (delta T2) analysis, but was included in pancreas volume measurements. Sensitivity analysis of the delta T2 data set did not indicate a different conclusion (P=0.025). Both possible contrast-related reactions were mild and without sequelae.

Region selection for T2 and T2* measurements. When determining region of interest for T2 and T2* measurements in the pancreas, preference was given for region selection within the anatomic head over the body or tail, with the region of interest selected encompassing at least 80% of the area of the anatomic section, while avoiding nonspecific susceptibility artifact from adjacent bowel or susceptibility from adjacent lymph nodes or other areas of high delta T2 or T2* external to the pancreas. If such a region of interest could not be placed within a given anatomic region then the next anatomic area within the pancreas would be attempted until

such a region could be placed. Such regions of interest could be identified for all study subjects on T2 sequences with high inter-observer agreement in T2 measurements between two independent readers (r^2=0.86). Quality review of the T2* sequences indicated that they were severely limited by nonspecific susceptibility artifact, obscuring the region of the pancreas. The T2* sequences were considered uninterpretable even after unmasking and were thus excluded from the final analysis.

Pancreas volume measurements. A post-contrast 3D-VIBE sequence, with freehand annotation of the pancreas, was used for volume estimations as described in Methods. Analysis in a randomly selected subgroup (5 patients and 5 controls) using the analogous 48-hour delayed contrast sequence demonstrated a mean volume difference of only 0.13 mL (95% CI -1.3 to 1.6 mL) with a maximum absolute difference of less than 6% total volume. Pancreas volume index was calculated by dividing the pancreatic volume by the body surface-area as determined by the formula of DuBois (1).

HLA Typing. The Roche Diagnostics T1D Linear Array assay used for HLA typing detects all the DRB1 group types (DR1-DR10) with 2 DRB1 “dual probes” that distinguishes DRB1*0403 (negatively associated) from DRB1*0407 (positively associated). There are 7 DQB1 probes in the assay that detect DQB1*0201 (in linkage disequilibrium with DR3), 0301, 0302 (in linkage disequilibrium with DR4, 0302 is associated with T1D), 0402 (in linkage disequilibrium with DR8) and 0602 (in linkage disequilibrium with DR2 and negatively associated with T1D). Other DQB1

alleles are not detected by the assay due to limited number of DQB1 probes on the testing strips.

Autoantibodies. Anti- insulin, GAD, and IA2 antibodies were assayed via radioimmunoassay, as previously described in Vardi et al. (2), Grubin et al. (3), and Payton et al. (4) respectively.

References

(1) Dubois D, DuBois E. A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med* 1916;17:863-871.

(2) Vardi P, Dib SA, Tuttleman M et al. Competitive insulin autoantibody RIA: Prospective evaluation of subjects at high risk for development of Type I diabetes mellitus. *Diabetes* 1987;36:1286-1291.

(3) Grubin CE, Daniels T, Toivola B et al. A novel radioligand binding assay to determine diagnostic accuracy of isoform-specific glutamic acid decarboxylase antibodies in childhood IDDM. *Diabetologia* 1994;37:344-350.

(4) Payton MA, Hawkes CJ, Christie MR. Relationship of the 37,000- and 40,000-M(r) tryptic fragments of islet antigens in insulin-dependent diabetes to the protein tyrosine phosphatase-like molecule IA-2 (ICA512). *J Clin Invest* 1995;96(3):1506-1511.