# Is there any point to human prediction?

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## History of the SAM methods

Since CASP2 in 1996, I have done human-assisted protein structure predictions for CASP, and since CASP4 have had servers (SAM-T99. SAM-T02, SAM-T06, SAM-T08). One question of continuing interest is whether the enormous amount of work put into looking at predictions and trying to guide the programs has any real benefit.

At CASP4, our hand predictions were much better than our server predictions, but much of the improvement was automatable and has been incorporated into our newer servers. For CASP6, we were still doing better by hand than our server, but other servers were doing fairly well.

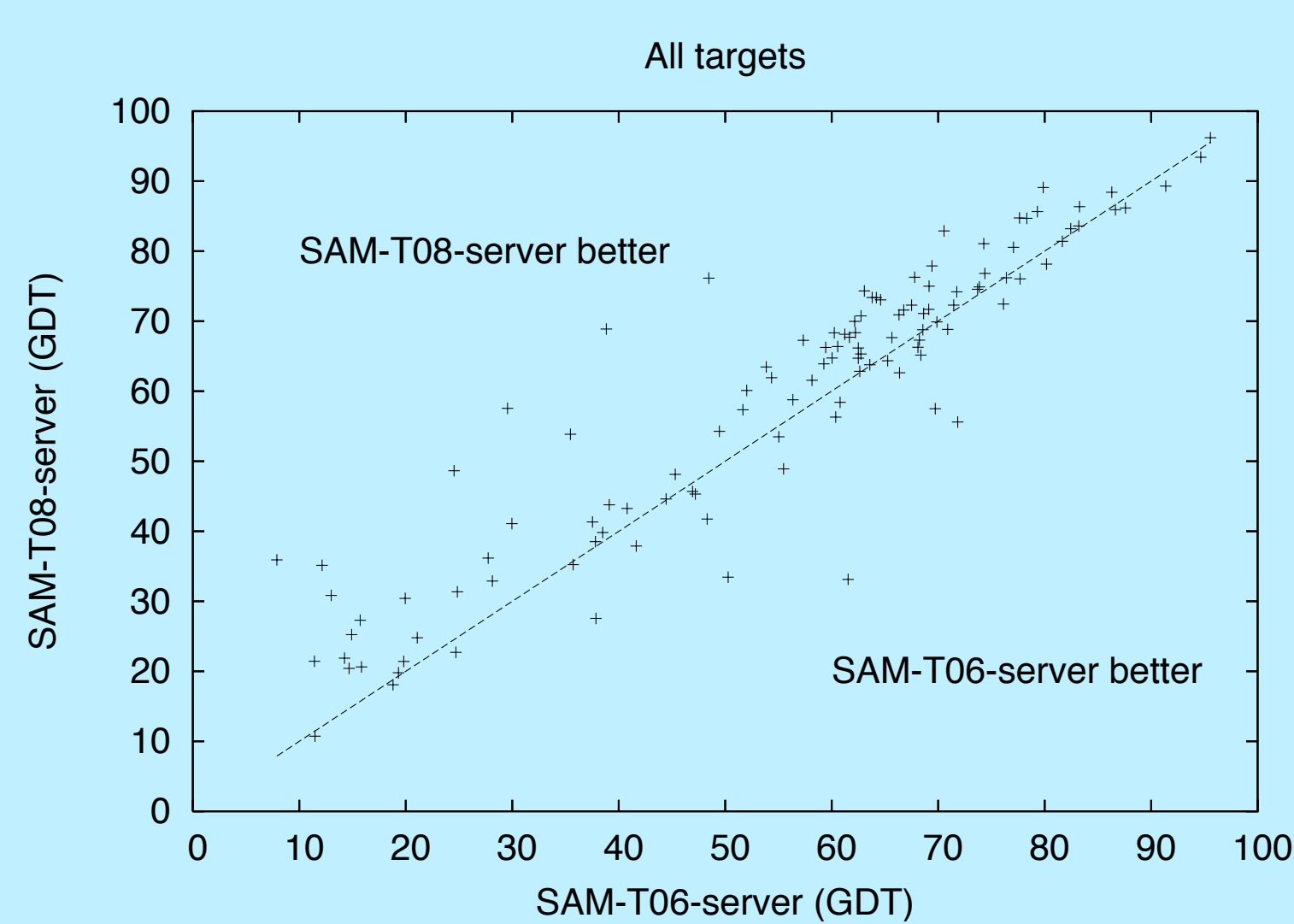At CASP8, we can see substantial improvement from the SAM-T06-server to the SAM-T08-server.



*Figure1. Comparison of GDT between SAM-T06-server and SAM-T08-server, using all targets and whole-chain GDT computations.*

We've also caught up with long-time rival Baker-Robetta (except for close comparative models).
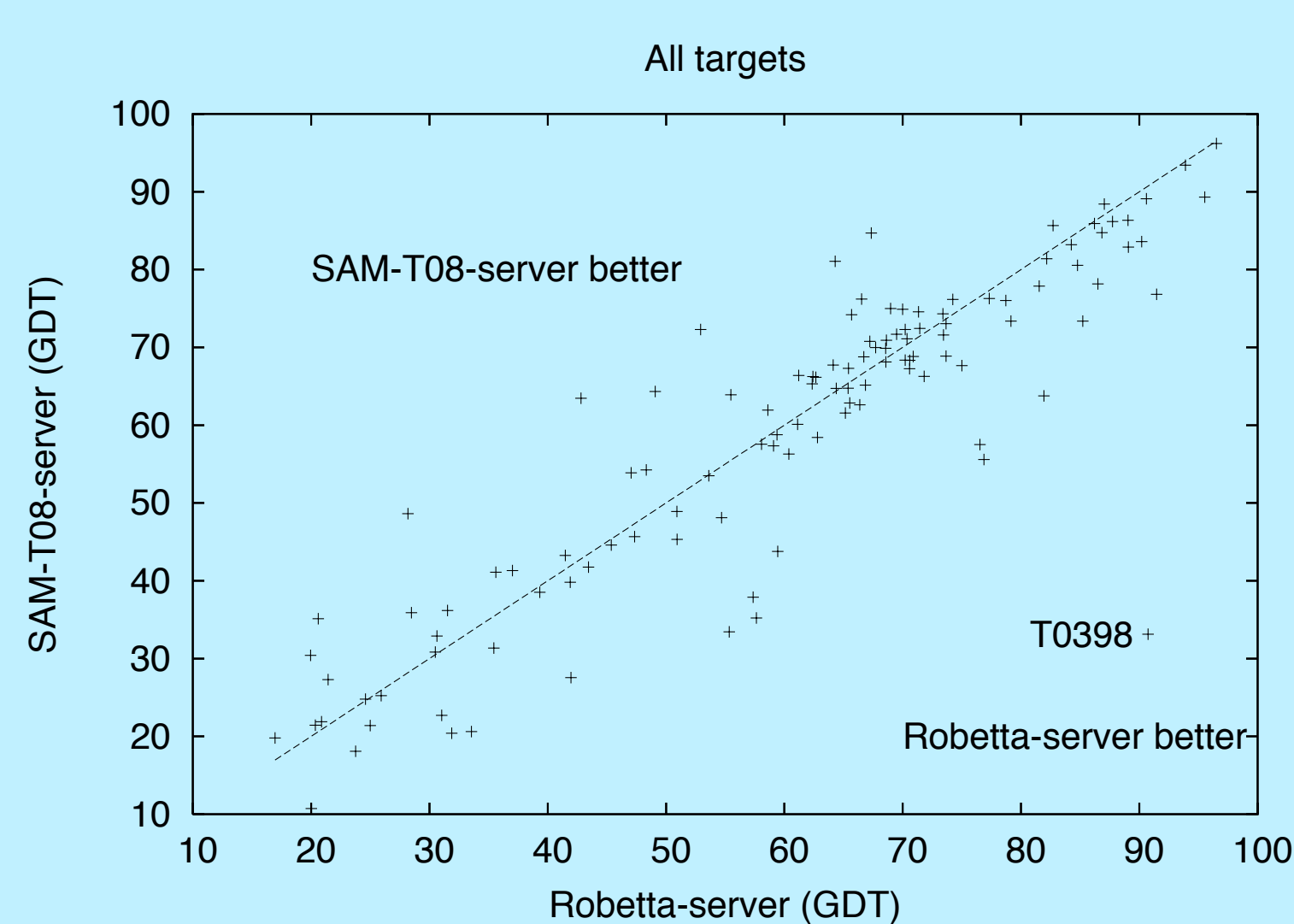


*Figure 2. Comparison of GDT between SAM-T08-server and BAKER-ROBETTA (whole-chain GDT, all models).*

Our hand predictions are still clearly better than our server predictions, which means that there is still a lot we haven't captured in our servers.
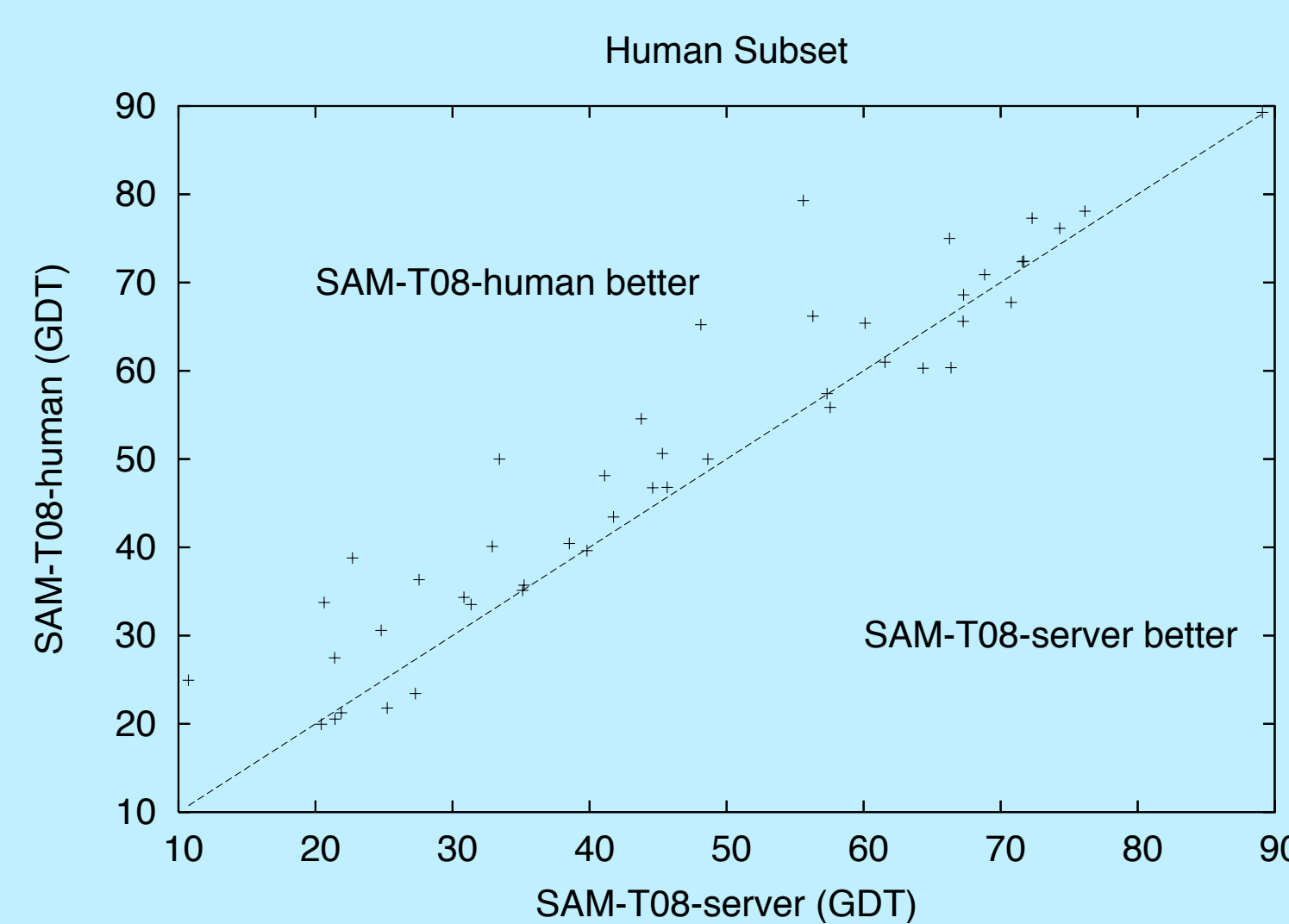


*Figure 3. Comparison of GDT between SAM-T08-server and SAM-T08-human model1, using whole-chain GDT for just the models requested of human predictors.*

## Model Quality Assessment

But our hand prediction was done after the servers were all finished and could use metaserver methods. The hand prediction was no better than just reporting the server model our MQAC method picked.
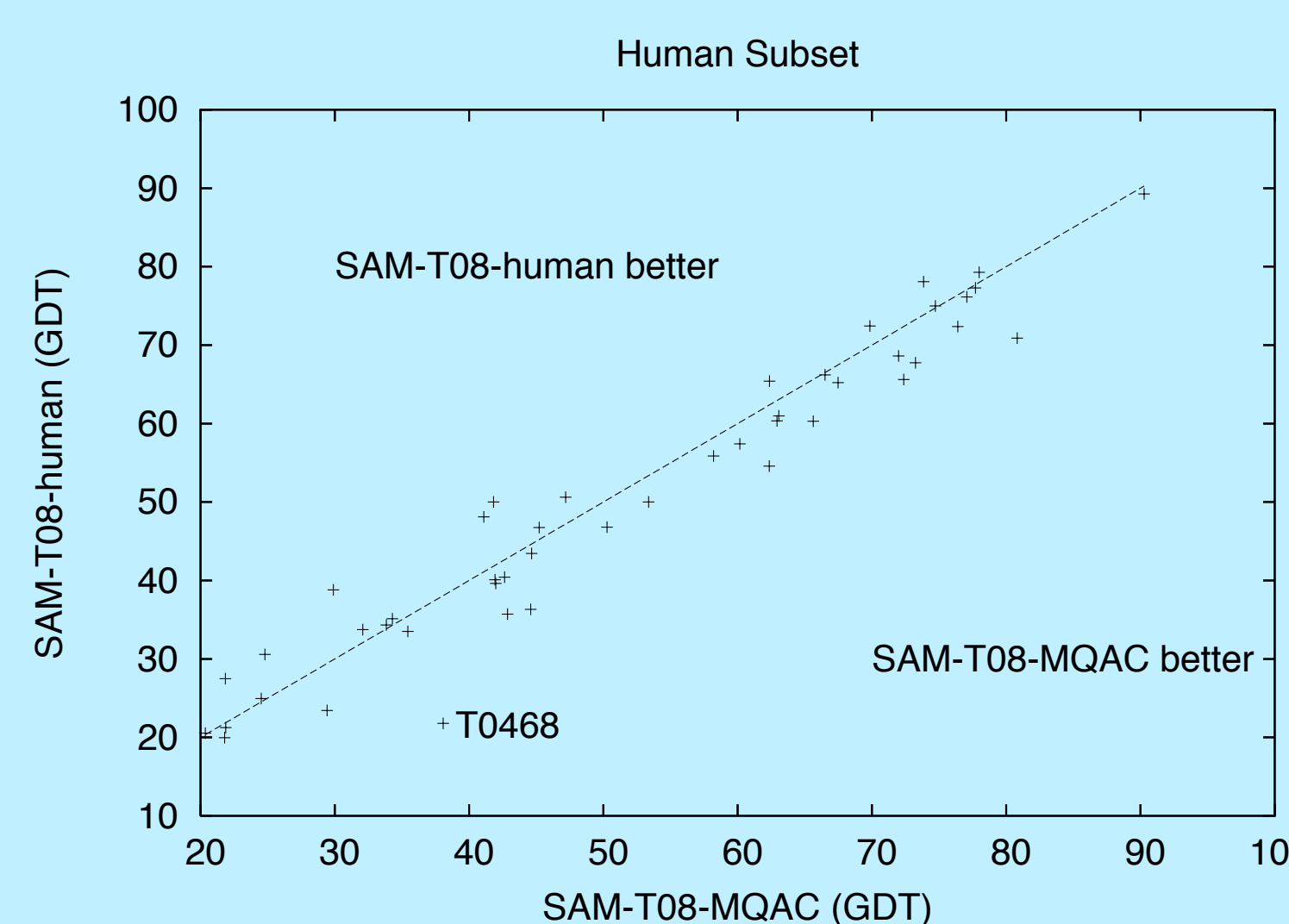


*Figure 4. Comparison of GDT between hand predictions and MQAC-based metaserver. The metaserver is better on the easy models, a little worse on the hard ones.*

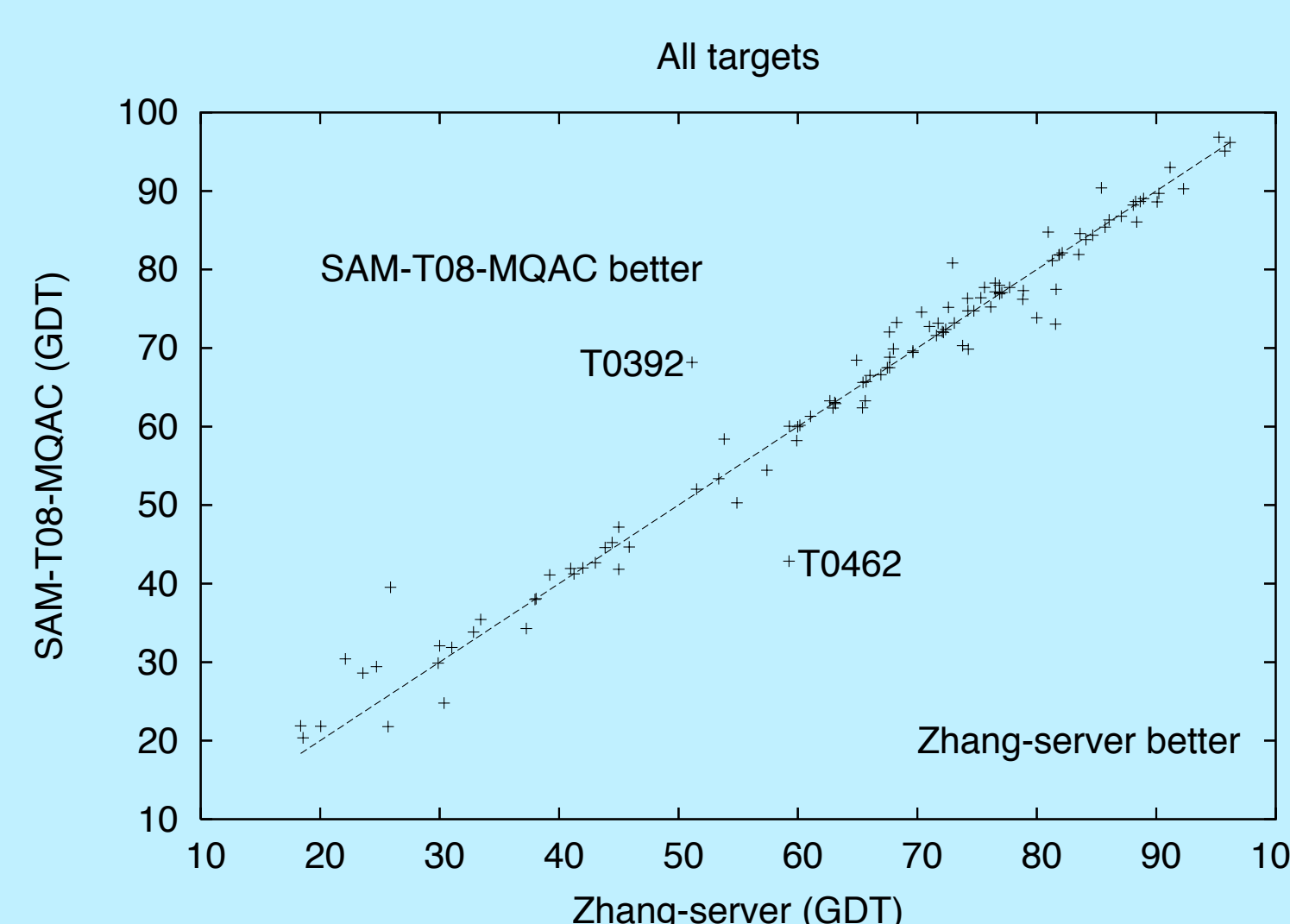But is even the metaserver worth working on? How does it compare to the server expected to do best based on CASP7?



*Figure 5. Comparison of GDT betwen MQAC as metaserver and Zhang-Server. There is a slight improvement from using the metaserver.*

## Future directions

Obviously, there is not much point to working on our hand predictions. But

should we focus on improving the alignments we generate? On choosing between alignments? On merging information from various alignments? On ab-initio and loop modeling? Or should we give up on trying to create a primary server and join the crowd doing almost identical metaservers?

Building a trivial sidechain-replacement model from our favorite alignment is not very good, so undertaker is adding something to simple alignment.
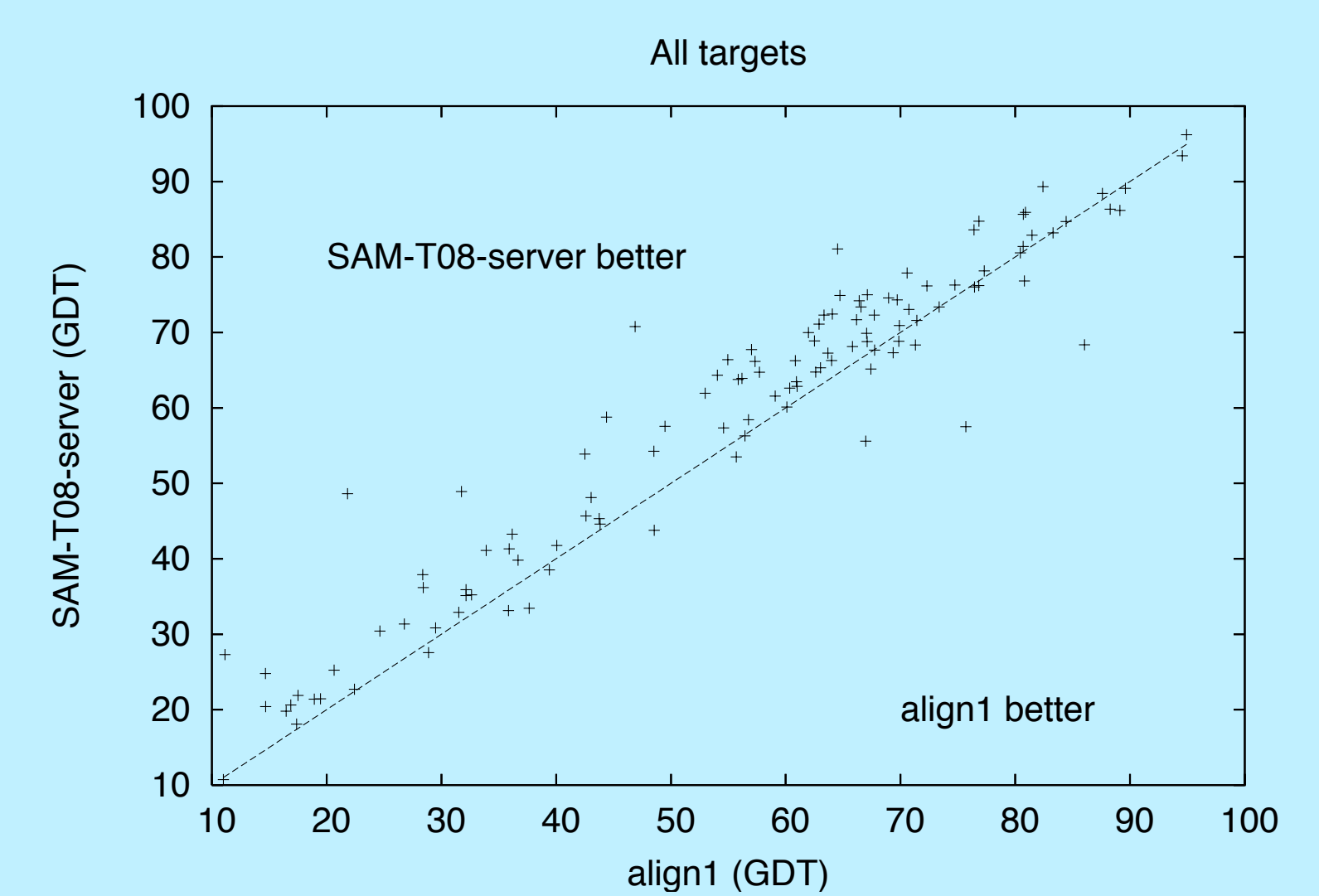


*Figure 6. Comparison of GDT between the SAM-T08-server and the 3-track local alignment for the lowest-Evalue template.*

But we are generating much better alignments, if we could just identify them.
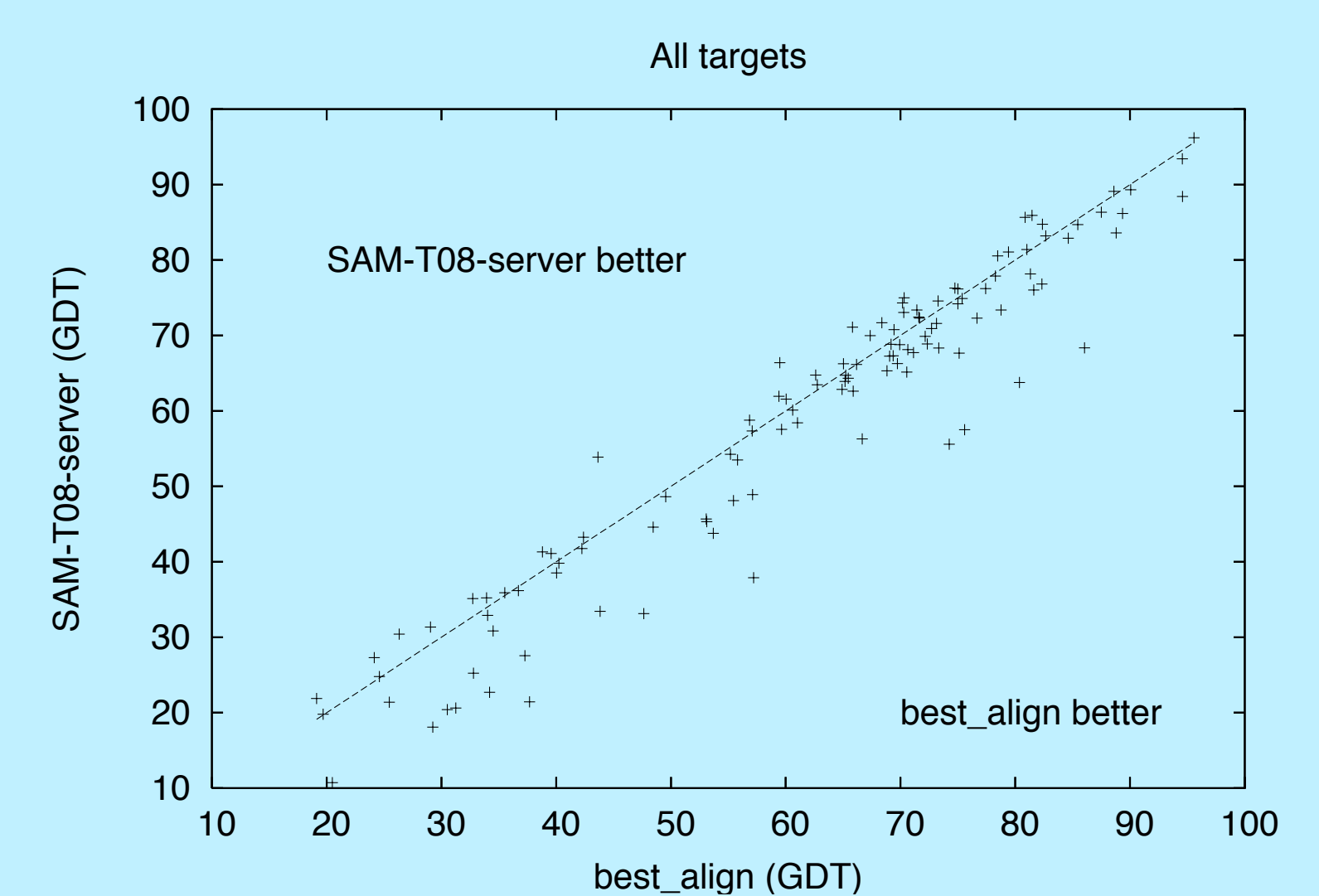


*Figure 7. Comparison of GDT between the SAM-T08-server and the lowest GDT alignment in the set of template alignments considered.*

But picking the best alignment out of the current set will not be enough.
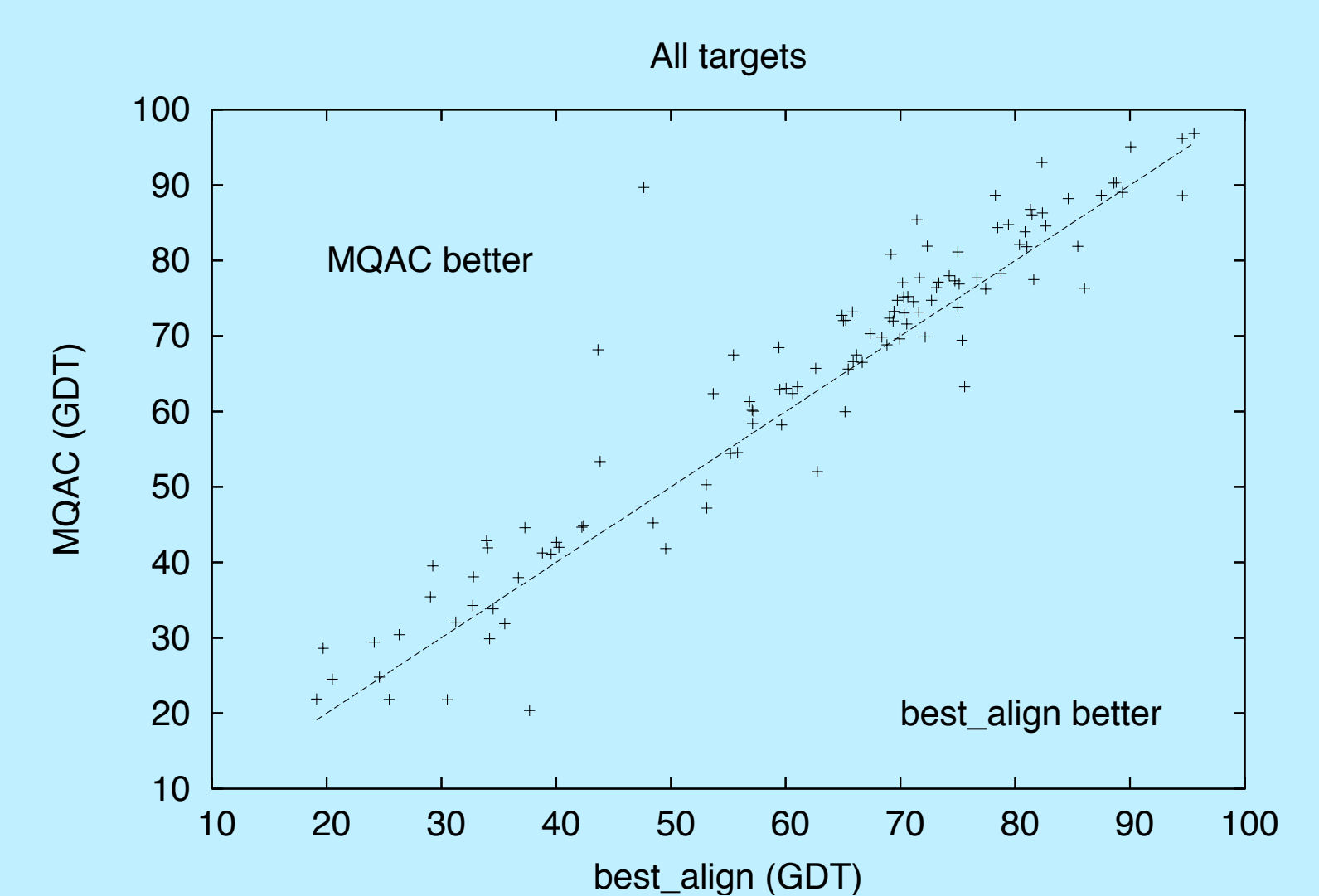


*Figure 8. Comparison of GDT between the MQAC-based metaserver and the lowest GDT alignment in the set of template alignments considered.*