

## LISA: A Clinical Information and Decision Support System for Collaborative Care in Childhood Acute Lymphoblastic Leukaemia . Jonathan Bury and Chris Hurt

In the UK, cancer care is typically organised according to a 'Hub and Spoke Model', in which a regional Treatment Centre collaborates with a network of local 'shared care' Units. Treatment Centres are typically large tertiary referral hospitals with expertise in the management of specific cancers and complex procedures. More routine components of an individual patient's treatment plan are delivered by a Cancer Unit - typically a district hospital more easily accessible to the patient.

Acute Lymphoblastic Leukaemia (ALL) is the commonest paediatric malignancy. Treatment of the disease can be viewed as comprising three phases – the *Induction* of clinical remission, the *Consolidation* of this remission, and subsequent *Continuing Therapy* (often referred to as maintenance therapy). ALL is unique amongst paediatric cancers in requiring such a long period of ongoing treatment and all evidence suggests that this period is the single most critical determinant of therapeutic outcome.

Currently in the UK, over 95% of children diagnosed with ALL are enrolled into the Medical Research Council UKALL 97/01 trial, and hence treatment follows the protocol defined by that trial. In this protocol, Continuing Therapy lasts between 24 months (girls) and 36 months (boys). The mainstay of treatment during this period is the regular administration of two oral chemotherapy agents, 6-mercaptopurine (given daily) and methotrexate (given weekly). There is great individual variation in response to these drugs, and dosages have to be continually adjusted to avoid inducing episodes of severe marrow suppression which would necessitate interruption of treatment to allow marrow recovery. These dosage adjustments are based on weekly Full Blood Counts (FBCs) which reflect the degree of recent marrow suppression. The UKALL 97/01 protocol includes rules describing how doses should be modified in response to these FBC results. These rules are moderately complex and their application requires knowledge not only of a child's most recent blood count but also of blood counts and chemotherapy dosages during the preceding twelve weeks.

Continuing Therapy is typically delivered collaboratively by Treatment Centres and associated Paediatric Oncology Shared Care Units (POSCUs). If dosage modifications are to be made in accordance with the treatment protocol, sharing of clinical information between Treatment Centers and POSCUs is essential.

The LISA (Leukaemia Intervention Scheduling and Advice) system has been developed as part of a collaboration between Cancer Research UK's Information Systems (Development) team, Children's Cancer Group (CCG) and Advanced Computation Laboratory (ACL). The CCG is based at the Royal London Hospital (RLH), UK, which is one of 22 Paediatric Oncology Treatment Centres in the UK accredited by the United Kingdom Children's Cancer Study Group (UKCCSG). An individual child with ALL is managed by the RLH in collaboration with one of a network of 60 POSCUs in south-east England.

A child's FBC and dosage history during Continuing Therapy is currently recorded on paper, with copies held both at the RLH and at the appropriate POSCU. At present, information is shared between sites using fax and telephone communication. We have developed a robust, centralised database for storing comprehensive data on interventions, scheduling, dosages and side-effects during treatment for all patients. We have also developed a web application for use by clinicians at point-of-care that provides a view of all blood results and dosage decisions made for a given patient during maintenance and also provides decision support on the appropriate dosages that should be prescribed next based on previous blood results and dose decisions and the current blood result.

LISA's decision support module was built using the *PROforma* decision support technology developed at Cancer Research UK. The *PROforma* language is a knowledge modelling system designed to allow the creation of formal, machine-readable

models of clinical protocols and guidelines. The language uses a task-based approach, which emphasises the relationships between the clinical procedures described, and the constraints which govern their scheduling and applicability to different patients in different circumstances. For this project, we created a *PROforma* model of Continuing Therapy which included all of the drugs used. We also modelled the rules associated with the decision needed to adjust the dose of oral chemotherapy drugs in response to weekly FBC tests. *PROforma* uses an argumentation-based approach to reasoning which enables a recommended course of action to be presented to the user together with patient-specific arguments for and against this proposal.

The UKALL 97/01 treatment protocol is, like all such protocols, subject to modification by trial co-ordinators as new evidence emerges. Such changes are likely to require modifications to the *PROforma* model of treatment. That model is entirely separate from other software components and accessed through an inference engine with defined operational semantics. This approach has enabled us to incorporate changes to the treatment protocol that have been made during the lifetime of the project without needing to re-engineer other components of the LISA system. The *PROforma* toolset includes Computer Assisted Software Engineering (CASE) tools to facilitate such authoring and editing *PROforma* models via a graphical user interface.

The potential for computerised decision-support systems to improve physician compliance within clinical trials, as well as supporting safety and efficiency, is well-recognised. However, there has been little progress in realising this potential – largely due to the difficulties of translating promising experimental systems into routine practice in complex clinical environments. In this project, we have been able to exploit an infrastructure developed to support electronic data gathering to additionally support the deployment of a decision-support system across a large number of institutions.

The decision-support tools developed have been targeted at recognised clinical needs - specifically dosage adjustments and scheduling of interventions during collaboratively delivered Continuing Therapy. A number of clinicians have expressed a desire to see the system extended to provide more detailed support for scheduling and co-ordination of interventions during Continuing Therapy. At present, the decision-support component informs users what tasks would normally be due in a given week, but this information is not patient-specific. We are exploring ways of extending the *PROforma* language and inference engine to enable users to query, for example, whether tasks are overdue or have been cancelled, or whether a task's intended rescheduling is within the bounds defined by the protocol.

### Architecture

The key software components of the LISA system are:

- An ORACLE database capable of representing comprehensive clinical information on each stage of treatment for individual children.
- A set of forms to allow data managers at Treatment Centers to view and modify information in that database.
- A web-based user interface to allow clinicians at Treatment Centers and POSCUs to view and enter clinical information during Continuing Therapy.
- A formal model of the trial protocol and an associated inference engine, used to provide decision support on dosing and scheduling during Continuing Therapy via the web interface.