ABSTRACT

Marker-assisted breeding value estimation is expected to increase the accuracy of estimated breeding values, especially for traits with low heritability. Several quantitative trait loci (QTL) have been found for somatic cell score and clinical mastitis. The objective of this study was to demonstrate marker-assisted breeding value estimation, combining data of genotyped and ungenotyped animals in a large pedigree population using either identical-by-descent (IBD) or identical-by-state (IBS) haplotypes for some previously identified QTL regions for somatic cell score and clinical mastitis in Finnish Ayrshire cattle. For both methods, QTL variances were estimated based on daughter yield deviations of genotyped bulls. The QTL explained only a small proportion of genetic variance, especially with IBS haplotypes. Using IBD haplotypes gave more reranking of bulls and cows than using IBS haplotypes. Cross-validation showed no increase in predictive ability when using IBS haplotypes compared with conventional breeding value estimation, whereas a decrease in predictive ability was observed with IBD haplotypes. Furthermore, computing time was lower and convergence was better with IBS haplotypes than with IBD haplotypes. In this study on mastitis resistance in Finnish Ayrshire, conventional breeding value estimation would be advocated because of the lack in improvement of accuracy and predictive ability when using marker-assisted breeding value estimation. However, in situations where IBS haplotypes would explain 10 to 20% or more of the genetic variance, marker-assisted breeding value estimation with IBS haplotypes may yield greater accuracy and predictive ability than conventional breeding value estimation.

Key words: mastitis, marker-assisted breeding value estimation, haplotype, ungenotyped animal

INTRODUCTION

Mastitis is one of the most costly diseases in dairy cattle. It has a low heritability, and recording is lacking in most countries. Therefore, in most countries, SCS, which is measured routinely in milk recording, is often used as an indicator trait for mastitis resistance. The advantage of SCS is that it is continuous and easy to measure, and it has higher heritability than mastitis resistance. Advanced use of the dynamics of SCS during lactation can further improve the accuracy of EBV for mastitis resistance (de Haas et al., 2008; Windig et al., 2010). In the Nordic countries, mastitis incidence is recorded on a national basis, making it possible to use direct information to predict EBV for mastitis resistance.

Another way to increase the accuracy of EBV for mastitis resistance is to perform marker-assisted breeding value estimation. Marker-assisted breeding value estimation increases accuracy mainly for genotyped animals, and the increase in accuracy is larger for low heritable traits compared with moderately or highly heritable traits (Lande and Thompson, 1990; Meuwissen and Goddard, 1996; Mulder et al., 2010a). Due to its low heritability, mastitis resistance is, therefore, a candidate trait for marker-assisted breeding value estimation. Considerable efforts have been made to find QTL for SCS and mastitis resistance (e.g., Schulman et al., 2004, 2009; Lund et al., 2007, 2008; Sahana et al., 2008; see review by Khatkar et al., 2004) or for SCS solely (e.g., Schrooten et al., 2000; Cole et al., 2009). In Nordic breeds, QTL have been reported on chromosomes 9, 14, and 18 (e.g., Schulman et al., 2004, 2009; Lund et al., 2007, 2008; Sahana et al., 2008). In other studies, QTL have been found on other chromosomes (Rupp and Boichard, 2003; Khatkar et al., 2004). Currently, high-density SNP chips are used for finding QTL; that is, genome-wide associations (e.g., Cole et al., 2009; Verbyla et al., 2010). Although some QTL have been found, marker-assisted breeding value estimation has not yet been implemented for mastitis resistance. One of the major challenges in this method is dealing with genotyped and ungenotyped animals in
one evaluation. One approach is to use identical-by-descent (IBD) haplotypes with use of IBD matrices to account for phase differences between QTL and markers. A second approach is to use identical-by-state (IBS) haplotypes, which do not require setting up large IBD matrices. Mulder et al. (2010a) developed a simple method to predict haplotypes of ungenotyped animals based on the mixed model method as presented in Gengler et al. (2007, 2008). With simulated data, they showed that with 4-marker haplotypes spaced at 0.1 cM, 90% of the QTL variance could be captured. However, so far this method has only been tested with simulated data and not directly compared with a method using IBD haplotypes. In addition, no study is known in which both methods were implemented in a large-scale, marker-assisted genetic evaluation.

The objective of this study was to demonstrate marker-assisted breeding value estimation combining data of genotyped and ungenotyped animals in a large pedigree population using IBD or IBS haplotypes, using some previously identified QTL regions for SCS and clinical mastitis in Finnish Ayrshire cattle.

**MATERIALS AND METHODS**

**Marker Data**

In this study, we focused on Finnish Ayrshire cattle. In previous studies, several bulls were genotyped for different regions of the genome to identify QTL (Viitala et al., 2003; Schulman et al., 2004; Sahana et al., 2008). These bulls were in a granddaughter design originating from 12 sires. In total, we had 3 generations of genotyped bulls, and birth years of these bulls ranged between 1975 and 2003. In total, genotypes of 1,157 bulls were available. We selected 10 markers belonging to 5 identified QTL regions being associated with either SCS or clinical mastitis (e.g., Viitala et al., 2003; Schulman et al., 2004; Sahana et al., 2008). Table 1 shows the number of genotyped bulls for each marker. In total, 498 bulls had genotypes for all markers and 640 bulls had at least one marker for each QTL region.

**Phenotypic Data**

From the national Finnish database, first-lactation records of cows were extracted from cows calving the first time between January 1, 1999, and December 31, 2008, a 10-yr period resulting in 591,596 records for lactation-average SCS, calculated as \(\text{ln(lactation-average SCC/1,000)}\); clinical mastitis between d \(-15\) and d \(50\) (CM1); and clinical mastitis between d \(51\) and d \(300\) (CM2). Table 2 shows some characteristics of the phenotypic data in relation to the genotyped bulls. The Finnish Ayrshire pedigree was pruned to include only cows with observations and cows and bulls that built up informative links between the cows with observations. An animal without observation was pruned if it had no offspring or if it had no ancestors and fewer than 2 offspring. The pruned pedigree contained 1,124,763 animals.

**Construction of IBS and IBD Haplotypes**

For the genotyped bulls, haplotypes were constructed and phased using Haprec (Windig and Meuwissen, 2004). The phased genotypes were subsequently used to construct either IBS or IBD haplotypes. The IBD haplotypes were constructed using linkage disequilibrium and linkage analysis information (LDLA) following Meuwissen and Goddard (2001) assuming an effective population size of 100 and 100 generations between the first generation in the pedigree and the founder generation. All markers on a chromosome were used to calculate IBD probabilities for each QTL region. In the case of QTL region 1 (QTL1), the QTL was assumed to be in the middle between microsatellite markers 2 (BMS2819) and 3 (INRA144) (Sahana et al., 2008); for QTL region 2 (QTL2), the QTL was assumed to be at the SNP marker (MAP4K4); for QTL region 3 (QTL3),

<table>
<thead>
<tr>
<th>Marker</th>
<th>Chromosome</th>
<th>Position (cM)</th>
<th>QTL designation</th>
<th>Bulls (n)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM4208</td>
<td>BTA9</td>
<td>74.0</td>
<td>1</td>
<td>739</td>
<td>Sahana et al. (2008)</td>
</tr>
<tr>
<td>BMS2819</td>
<td>BTA9</td>
<td>74.0</td>
<td>1</td>
<td>1,121</td>
<td>Sahana et al. (2008)</td>
</tr>
<tr>
<td>INRA144</td>
<td>BTA9</td>
<td>74.2</td>
<td>1</td>
<td>695</td>
<td>Sahana et al. (2008)</td>
</tr>
<tr>
<td>MAP4K4</td>
<td>BTA11</td>
<td>10.5</td>
<td>2</td>
<td>817</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>MNB40</td>
<td>BTA11</td>
<td>16.0</td>
<td>3</td>
<td>626</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>BM716</td>
<td>BTA11</td>
<td>17.9</td>
<td>3</td>
<td>708</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>DIK2653</td>
<td>BTA11</td>
<td>18.1</td>
<td>3</td>
<td>608</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>HELMTT44</td>
<td>BTA11</td>
<td>61.2</td>
<td>4</td>
<td>940</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>TGLA58</td>
<td>BTA11</td>
<td>63.1</td>
<td>4</td>
<td>1,126</td>
<td>Schulman et al. (2009)</td>
</tr>
<tr>
<td>TGLA227</td>
<td>BTA18</td>
<td>110.0</td>
<td>5</td>
<td>1,110</td>
<td>Viitala et al. (2003)</td>
</tr>
</tbody>
</table>
the QTL was assumed to be between microsatellite markers 1 (MNB40) and 2 (BM716), because of the large distance and the fact that markers 2 (BM716) and 3 (DIK2653) are very close to each other. For QTL region 4 (QTL4), the QTL was assumed to be between the 2 microsatellite markers (HELMT44 and TGLA58); and for QTL region 5 (QTL5), the QTL was assumed to be at the microsatellite marker (TGLA227), in absence of flanking markers. Distances between markers were based on Haldane’s mapping function (Haldane, 1919). For animals with no genotypes, haplotypes and IBD-matrices were constructed using the Fernando and Grossman (1989) rules.

The IBS haplotypes were constructed based on the phased genotypes and on the alleles of the different microsatellites. For QTL2, the IBS haplotype was based on a single SNP allele and for QTL5 the IBS haplotypes were based on different alleles of the microsatellite. For some bulls, no genotypes were available for certain markers in a QTL region. It was assumed that those bulls had a zero allele for those markers not genotyped. Subsequently, markers were concatenated and renumbered from 1 to the maximum number of haplotypes. In this way, we constructed 143, 2, 163, 43, and 11 haplotypes for QTL 1, 2, 3, 4, and 5, respectively. The next stage was to predict the number of haplotype alleles (nhc) for ungenotyped animals using the method described in Mulder et al. (2010a).

Variance Component Estimation for Each QTL Region

The QTL variances were estimated, because QTL effects were modeled as random effects with either IBS or IBD haplotypes. The QTL variances were estimated using daughter yield deviations (DYD) of the genotyped bulls with effective daughter contributions (EDC) as weights on the residual variance to account for differences in accuracy of the DYD. The calculated DYD (Mrode and Swanson, 2004) and EDC (Fikse and Banos, 2001) were based on all Finnish phenotypic data of 1.3 million records used in the joint Nordic evaluation. For the variance component analysis, we used only bulls that had at least one marker for each QTL region genotyped (640 bulls).

Three univariate analyses were done in ASREML (Gilmour et al., 2006) fitting the model

\[
DYD = \mu + \sum_{i=1}^{5} (h_{i,p} + h_{i,m}) + e,
\]

where \(DYD\) is the daughter yield deviation for SCS, CM1, or CM2; \(\mu\) is the overall mean; \(u_{pol}\) is the random polygenic effect \(N(\mathbf{0}, \mathbf{A}\sigma_{pol}^2)\); \(\mathbf{A}\) is the additive genetic or numerator relationship matrix and \(\sigma_{pol}^2\) is the polygenic genetic variance; \(h_{i,p}\) (\(h_{i,m}\)) is the random paternal (maternal) haplotype effect for QTL \(i\); and \(e\) is the random residual \(N(\mathbf{0}, \mathbf{D}\sigma_e^2)\); \(\mathbf{D}\) is the diagonal matrix with the reciprocal of EDC of each bull (Mrode, 2005) and \(\sigma_e^2\) is the residual variance. When using IBD haplotypes the haplotype effects were assumed to be distributed as \(N(\mathbf{0}, \mathbf{IBD}\sigma_{h_i}^2)\), where \(\mathbf{IBD}\) is the IBD matrix based on LDLA for QTL \(i\), and \(\sigma_{h_i}^2\) is the haplotype variance of QTL \(i\). When using IBS haplotypes, the haplotype effects were assumed to be independent \(N(\mathbf{0}, \mathbf{I}\sigma_{h_i}^2)\). The estimated variances per QTL were calculated as proportions of the total genetic variance. Multivariate analyses did not converge.

Breeding Value Estimation

Three multivariate models were applied for breeding value estimation: conventional breeding value estima-
tion (CONBLUP), marker-assisted breeding value estimation with IBD haplotypes (MABLUP-IBD), and marker-assisted breeding value estimation using IBS haplotypes (MABLUP-IBS). A multivariate model was used for breeding value estimation. Effects in the CONBLUP model were based on the Nordic evaluation before 2010 (Johansson et al., 2006):

\[ y = H5Y + AGE + YM + hy + u_{pol} + e, \]

where \( y \) is SCS, CM1, and CM2; \( H5Y \) is the fixed effect for herd-5-yr period; \( AGE \) is fixed age at first calving as a fixed class effect; \( YM \) is the fixed year-month effect; \( hy \) is the random herd-year effect \([MVN(0, I \otimes HY)]\), where \( MVN = \) multivariate normal; \( u_{pol} \) is the random polygenic effect \([MVN(0, A \otimes G)]\); \( e \) is the random residual \([MVN(0, I \otimes R)]\); \( G \) is the polygenic variance-covariance matrix; \( HY \) is the diagonal variance-covariance matrix of herd-year effects; \( I \) is the identity matrix; and \( R \) is the residual variance-covariance matrix.

The model for MABLUP-IBD was the combination of model [2] with model [1]:

\[ y = H5Y + AGE + YM + hy + u_{pol} + \sum_{i=1}^{5} (h_{i,p} + h_{i,m}) + e, \]

where \( h_{i,p} (h_{i,m}) \) is the paternal (maternal) haplotype; \([MVN(0, IBD_i \otimes H_i)]\) and \( H_i \) is the variance-covariance matrix for QTL \( i \). The haplotype EBV was \( \sum_{i=1}^{6} (h_{i,p} + h_{i,m}) \), and the total EBV was calculated as \( u_{pol} + \sum_{i=1}^{6} (\hat{h}_{i,p} + \hat{h}_{i,m}) \), the sum of the haplotype EBV and polygenic effect.

The model for MABLUP-IBS was model [2] extended with a regression on the number of haplotype alleles (see Mulder et al., 2010a) and therefore slightly differently parameterized than model [1], but equivalent to model [1]:

\[ y = H5Y + AGE + YM + hy + u_{pol} + \sum_{i=1}^{5} n_i \hat{h}_{c_{ij}} \times h_{ij} + e, \]

where \( n_i \hat{h}_{c_{ij}} \) is the number of haplotype alleles for haplotype \( j \) of QTL \( i \); \( h_{ij} \) is the regression coefficient for haplotype \( j \) of QTL \( i \) \([MVN(0, I \otimes H_i)]\); and \( n_i \) is the number of haplotypes used for QTL \( i \). Because of the large number of haplotypes for QTL 1, 3, and 4, and to limit computing time, we selected for each animal the 20 haplotypes with the largest \( \hat{h}_{c_{ij}} \), because the others had rather small values, close to zero, which would have had a negligible effect on breeding value estimation. When using the 20 haplotypes with the largest \( \hat{h}_{c_{ij}} \), the average sum of \( n_i \hat{h}_{c_{ij}} \) was 1.76, 1.42, and 1.96, respectively for QTL1, QTL3, and QTL4, indicating that most of the haplotype information was captured. The haplotype EBV was \( \sum_{i=1}^{5} \sum_{j=1}^{n} (n_i \hat{h}_{c_{ij}} \times h_{ij}) \) and the total EBV was calculated as \( u_{pol} + \sum_{i=1}^{5} \sum_{j=1}^{n} (\hat{h}_{c_{ij}} \times h_{ij}) \), the sum of the haplotype EBV and polygenic effect.

For cows, we performed a 10-fold cross-validation where 10% of the cow phenotypes were deleted. For each cow with phenotypes, the phenotypes were set to missing in 1 of the 10 reduced data sets. To limit
computing time, we performed only CONBLUP and MABLUP-IBS on each of the 10 reduced data sets. Instead of calculating correlations between EBV and observed phenotypes for validation cows, which is not very meaningful for binomial traits, we calculated the incidence of CM1 and CM2 per 10%-quantile of EBV, either from CONBLUP or the total EBV from MABLUP-IBS. The incidence was averaged across the 10 replicates.

**RESULTS**

**Variance Component Estimation for Each QTL Region**

Estimated variance components and the proportions of genetic variance explained by QTL were sensitive to the model used and the markers used to construct IBD matrices (results not shown). For instance, excluding the polygenic effect from equation [1] resulted in extremely high proportions of genetic variance explained, up to 71.6%, due to capturing family-specific effects rather than true QTL effects of the genetic variance (e.g., Kennedy et al., 1992). In addition, the genetic variance explained by QTL2 with IBD depended largely on whether the IBD matrices were based on the single SNP or on all markers on chromosome 11. When the IBD matrices were constructed using only the single SNP (MAP4K4) on chromosome 11, the SNP explained 57.2% of the genetic variance, whereas it explained very little variance when the IBD matrices were constructed using all markers on chromosome 11.

The final estimated QTL variances (Table 3) were estimated with either IBD or IBS haplotypes and expressed as proportions of the total genetic variance (Table 4). The model with IBD haplotypes explained more genetic variance than the model with IBS haplotypes. In both models, QTL1 and QTL2 explained hardly any genetic variance, whereas QTL4 and QTL5 explained substantial proportions of genetic variance, especially for CM1 and CM2. Strikingly, QTL3 explained 13.1% of the genetic variance for CM1 when using IBD, whereas it explained hardly any variance with IBS. Standard errors on the estimated variances per QTL were large relative to the estimate, indicating low precision of the estimated variance components. The estimated residual variances as well as the total amount of genetic variance were very similar across models and similar as well to the estimates by Negussie (MTT Agrifood Research Finland, Biotechnology and Food Research, Genetics Research, Jokioinen, Finland, personal communication). Note that the estimated polygenic and QTL variances were one-quarter of the true polygenic or QTL variance because of using DYD.

**Breeding Value Estimation**

Table 5 shows correlations between conventional EBV and marker-assisted total, polygenic, and haplotype EBV using either IBD or IBS haplotypes. Correlations between conventional EBV and total EBV were higher when using IBS haplotypes than when using IBD haplotypes, indicating less reranking; reranking was smallest for SCS. Correlations were quite similar for bulls and cows. The correlation between haplotype EBV and conventional EBV was high for IBD haplotypes but low for IBS haplotypes. Furthermore, the correlations between haplotype EBV of both methods were between 0.12 and 0.32, indicating that both methods are different and that IBD haplotypes may capture family-specific effects rather than QTL effects. It can be concluded that IBD haplotypes caused more reranking than IBS haplotypes; IBD haplotypes also explained more genetic variance than IBS haplotypes.

**Predictive Ability**

**Bulls.** In all cases, the results (Table 6) of cross-validation based on bulls indicated that predictive ability was lower for MABLUP than for CONBLUP, except for CM2 in MABLUP-IBS, where it was slightly higher. The correlations between EBV of the full and reduced data sets were, in general, high for these traits with a low heritability, because pedigree information was still weighted heavily in both sets of EBV, inflating the correlation due to partly using the same information. Correlations between IBS haplotype EBV of the full and reduced data sets were very high (>0.92), whereas correlations between the IBD haplotype EBV of the full and reduced data sets were quite low. This indicates that effects of IBS haplotypes had higher predictive ability than IBD haplotypes.

**Cows.** Figure 1A and 1B show, respectively, the incidence of CM1 and CM2 for 10%-quantiles of the EBV for CM1 and CM2 when all data were used. The figures show a large difference in incidence between the cows with the highest (unfavorable) and the lowest (favorable) EBV. For CM1 (Figure 1A), differences between methods were very small. For CM2 (Figure 1B), however, MABLUP-IBS had a higher incidence for cows with the highest EBV than CONBLUP and MABLUP-IBD. In this case, the cows’ own phenotypes were used to estimate the EBV. In Figure 2, the incidence is shown for cross-validation cows, whose phenotypes were set to missing in the breeding value estimation using CONBLUP or MABLUP-IBS. Although the variation in incidence of CM1 and CM2 is much smaller than in Figure 1, Figure 2 shows that EBV were predictive for mastitis incidence, indicating that cows with
higher EBV had higher incidence of mastitis. The difference between CONBLUP and MABLUP-IBS was, however, negligible, indicating that both methods had similar predictive ability for mastitis incidence. When the incidence of CM1 and CM2 was calculated per 10%-quantile of haplotype EBV, the difference in incidence of CM1 and CM2 between cows with the highest and lowest EBV was much smaller than for total EBV, but still highly significant \((P < 0.001; \text{Student's } t\text{-test})\), indicating that the haplotypes capture QTL effects associated with clinical mastitis.

**DISCUSSION**

The aim of this study was to demonstrate marker-assisted breeding value estimation for mastitis resistance in Finnish Ayrshire cattle, combining data of genotyped and ungenotyped animals using previously identified QTL regions. Furthermore, we compared marker-assisted EBV using either IBD or IBS haplotypes to conventional EBV and investigated the predictive value of these EBV. With both methods, it was possible to deal with ungenotyped and genotyped animals in a single evaluation. Therefore, both methods are able to generate benefits, especially for genotyped animals. In this particular situation, marker-assisted breeding value estimation performed, however, similar to or worse than conventional breeding value estimation.

The selection of the markers and QTL regions was based on previous research, which made use in part of the same data. The focus of our study was marker-assisted breeding value estimation, and therefore we focus here only on differences and similarities by means of analyzing the estimated variances per QTL region. The QTL on BTA9 at \(~74\text{ cm}\) explained hardly any genetic variance, even when it was the only QTL in the model, as in Sahana et al. (2008). Sahana et al. (2008) found that this QTL was not significant in Finnish Ayrshire cattle, whereas it was significant in Danish Red or in analyses across Nordic red breeds. In this study, we found that QTL3 (\(~17\) to \(~18\) cm on BTA11) explained a substantial proportion of genetic variance in CM1 with IBD haplotypes, which confirmed the peaks found at \(~62\text{ cm}\) in Schulman et al. (2009), but was in disagreement with Lund et al. (2007), who found only a peak for SCS.

The IBS haplotypes explained much less genetic variance than the IBD haplotypes. It might be that IBD haplotypes captured family-specific effects beyond

### Table 3. Variance components (SE in parentheses) for a conventional BLUP model and for MABLUP-IBD and MABLUP-IBS for 5 selected QTL regions

<table>
<thead>
<tr>
<th>Variance</th>
<th>CONBLUP</th>
<th>MABLUP-IBD</th>
<th>MABLUP-IBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polygenic</td>
<td>4.49E−03</td>
<td>4.49E−03</td>
<td>4.49E−03</td>
</tr>
<tr>
<td>QTL1</td>
<td>6.33E−06</td>
<td>6.33E−06</td>
<td>6.33E−06</td>
</tr>
<tr>
<td>QTL2</td>
<td>5.83E−05</td>
<td>5.83E−05</td>
<td>5.83E−05</td>
</tr>
<tr>
<td>QTL3</td>
<td>3.34E−05</td>
<td>3.34E−05</td>
<td>3.34E−05</td>
</tr>
<tr>
<td>QTL4</td>
<td>1.72E−01</td>
<td>1.72E−01</td>
<td>1.72E−01</td>
</tr>
<tr>
<td>Residual</td>
<td>8.57E−02</td>
<td>8.57E−02</td>
<td>8.57E−02</td>
</tr>
</tbody>
</table>

See Table 1 for locations of QTL. SCS = lactation-average SCS; CM1 = clinical mastitis between d −15 and 50; CM2 = clinical mastitis between d 51 and 300. CONBLUP = conventional BLUP; MABLUP-IBD = marker-assisted breeding value estimation with identical-by-descent haplotypes; MABLUP-IBS = marker-assisted breeding value estimation with identical-by-state haplotypes. Variance component was bounded to keep the estimate positive; estimate was effectively zero.
pure QTL effects. Because the numerator relationship matrix and the IBD matrix were partly overlapping, especially with poor or missing marker information, disentangling polygenic and QTL effects might be challenging. Overestimation of QTL effects due to population stratification is a generic problem in QTL mapping (e.g., Kennedy et al., 1992; Martinez et al., 1999; Wang and Elston, 2005). Neuner et al. (2009) showed with simulations that the QTL variance is slightly overestimated when using daughter yield deviations with an IBD model. Nevertheless, with both methods, the 5 QTL used explained a small proportion of the genetic variance, and therefore SCS and clinical mastitis are likely to be affected by many genes, making genome-wide evaluation approaches more effective than marker-assisted breeding value estimation with a few putative QTL regions. Cross-validation studies for the Nordic red dairy cattle have shown that genome-wide evaluation yields good accuracy for udder health, but the accuracy is smaller than in Holstein cattle (Brøndum et al., 2010).

In this study, we performed 2 types of cross-validation: one based on bulls and one based on cows. Cross-validation with bulls is intended to give the predictive ability of EBV of young bulls before entering progeny testing, but clearly, in this case, the sample size of 104 bulls was quite small. The cross-validation showed that IBD haplotype effects were estimated with much lower accuracy than IBS haplotypes, which caused the lower correlation obtained for total EBV compared with CONBLUP. For all models, correlations between EBV of the reduced set and the full data set were inflated, because both EBV relied heavily on pedigree information. The cross-validation with cows showed that EBV are predictive of mastitis incidence on a phenotypic level, but the conventional breeding value estimation did not differ from marker-assisted breeding value estimation with IBS haplotypes in levels of incidence based on 10%-quantiles of EBV. This might be because the IBS haplotypes explained only a small proportion of the genetic variance. On the other hand, it shows that marker-assisted breeding value estimation with IBS haplotypes is quite robust and should at least give increased accuracy for genotyped animals, such as occurred for CM2 in genotyped bulls. Based on the simulation in Mulder et al. (2010a), it is expected that MABLUP-IBS would increase the accuracy of EBV for genotyped animals when the IBS haplotypes explain 10

Table 4. Estimates of variance components using identical-by-descent (IBD) or identical-by-state (IBS) haplotypes as a proportion to the total genetic variance for 5 selected QTL regions.

<table>
<thead>
<tr>
<th>Method</th>
<th>Trait</th>
<th>QTL1</th>
<th>QTL2</th>
<th>QTL3</th>
<th>QTL4</th>
<th>QTL5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD</td>
<td>SCS</td>
<td>0.003</td>
<td>0.000</td>
<td>0.026</td>
<td>0.000</td>
<td>0.015</td>
<td>0.044</td>
</tr>
<tr>
<td></td>
<td>CM1</td>
<td>0.000</td>
<td>0.000</td>
<td>0.131</td>
<td>0.014</td>
<td>0.016</td>
<td>0.161</td>
</tr>
<tr>
<td></td>
<td>CM2</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.064</td>
<td>0.030</td>
<td>0.094</td>
</tr>
<tr>
<td>IBS</td>
<td>SCS</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.009</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>CM1</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.011</td>
<td>0.003</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>CM2</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.026</td>
<td>0.024</td>
<td>0.049</td>
</tr>
</tbody>
</table>

1See Table 1 for locations of QTL.
2SCS = lactation-average SCS; CM1 = clinical mastitis between d −15 and 50; CM2 = clinical mastitis between d 51 and 300.

Table 5. Correlations between conventional EBV (Con) and marker-assisted total EBV (Tot), polygenic EBV (Pol), and haplotype EBV (Hap) for bulls and cows for SCS, CM1, and CM2 using identical-by-descent or identical-by-state haplotypes.

<table>
<thead>
<tr>
<th>Method</th>
<th>Trait</th>
<th>Bulls</th>
<th>Cows</th>
<th>Con-Tot</th>
<th>Con-Pol</th>
<th>Con-Hap</th>
<th>Con-Hap</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Con-Tot</td>
<td>Con-Pol</td>
<td>Con-Hap</td>
<td>Con-Hap</td>
</tr>
<tr>
<td>MABLUP-IBD</td>
<td>SCS</td>
<td>1.000</td>
<td>0.996</td>
<td>0.434</td>
<td>0.998</td>
<td>0.996</td>
<td>0.710</td>
</tr>
<tr>
<td></td>
<td>CM1</td>
<td>0.987</td>
<td>0.986</td>
<td>0.337</td>
<td>0.986</td>
<td>0.979</td>
<td>0.682</td>
</tr>
<tr>
<td></td>
<td>CM2</td>
<td>0.948</td>
<td>0.855</td>
<td>0.719</td>
<td>0.940</td>
<td>0.851</td>
<td>0.753</td>
</tr>
<tr>
<td>MABLUP-IBS</td>
<td>SCS</td>
<td>0.999</td>
<td>0.999</td>
<td>0.024</td>
<td>1.000</td>
<td>1.000</td>
<td>0.106</td>
</tr>
<tr>
<td></td>
<td>CM1</td>
<td>0.995</td>
<td>0.997</td>
<td>0.015</td>
<td>0.998</td>
<td>0.998</td>
<td>0.131</td>
</tr>
<tr>
<td></td>
<td>CM2</td>
<td>0.992</td>
<td>0.996</td>
<td>0.078</td>
<td>0.997</td>
<td>0.997</td>
<td>0.111</td>
</tr>
</tbody>
</table>

1Based on 341 bulls genotyped for all markers with a reliability of 0.80 or higher for SCS.
2MABLUP-IBD = marker-assisted breeding value estimation with identical-by-descent (IBD) haplotypes; MABLUP-IBS = marker-assisted breeding value estimation with identical-by-state (IBS) haplotypes.
3SCS = lactation-average SCS; CM1 = clinical mastitis between d −15 and 50; CM2 = clinical mastitis between d 51 and 300.
to 20% of the genetic variance. The limited or absent increase in predictive ability for ungenotyped animals is in agreement with the simulation results in Mulder et al. (2010a). In addition, Gengler et al. (2008) found no increase in accuracy for SCS with gene-assisted breeding value estimation when using a candidate gene that explained a very small amount of genetic variance.

Many countries are currently implementing genome-wide evaluations in dairy cattle, with the advantage that high-density SNP chips capture larger amounts of genetic variance than traditional QTL approaches. Furthermore, genome-wide evaluation eliminates the need to find QTL, because the method assumes either that all SNP contribute equally to the genetic variance (GBLUP) or that the model decides itself which SNP will have large and which will have small effects (e.g., BayesB or BayesC approaches; Meuwissen et al., 2001; Gianola et al., 2009). However, marker-assisted breeding value estimation for several QTL may still be of interest for some species in which genotyping animals by using high-density SNP chips is too expensive. Another application would be for cases in which a major QTL exists and where a combination of GBLUP and the major gene effect modeled separately is as effective as the BayesB or BayesC approach.

We showed the feasibility of estimating marker-assisted breeding values in a large dairy cattle population that consisted of genotyped and ungenotyped animals. A model with IBD haplotypes and IBD matrices was computationally more demanding in many aspects than a model using IBS haplotypes without the use of additional IBD matrices. First, making the IBD matrix

### Table 6. Cross-validation for bulls born in 2002 and 2003 with all genotypes and with a reliability of at least 0.80 for SCS when using all data with conventional breeding value estimation (CONBLUP) and marker-assisted breeding value estimation using identical-by-descent or identical-by-state haplotypes (MABLUP-IBD and MABLUP-IBS, respectively)

<table>
<thead>
<tr>
<th>Method</th>
<th>Type of EBV</th>
<th>SCS</th>
<th>CM1</th>
<th>CM2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONBLUP</td>
<td>Conventional</td>
<td>0.512</td>
<td>0.488</td>
<td>0.569</td>
</tr>
<tr>
<td>MABLUP-IBD</td>
<td>Haplotype</td>
<td>0.405</td>
<td>0.667</td>
<td>0.433</td>
</tr>
<tr>
<td>MABLUP-IID</td>
<td>Polygenic</td>
<td>0.533</td>
<td>0.455</td>
<td>0.520</td>
</tr>
<tr>
<td>MABLUP-IIB</td>
<td>Total</td>
<td>0.502</td>
<td>0.485</td>
<td>0.418</td>
</tr>
<tr>
<td>MABLUP-IBS</td>
<td>Haplotype</td>
<td>0.928</td>
<td>0.983</td>
<td>0.971</td>
</tr>
<tr>
<td>MABLUP-IID</td>
<td>Polygenic</td>
<td>0.516</td>
<td>0.491</td>
<td>0.578</td>
</tr>
<tr>
<td>MABLUP-IIB</td>
<td>Total</td>
<td>0.506</td>
<td>0.488</td>
<td>0.574</td>
</tr>
</tbody>
</table>

1Correlations between conventional, haplotype, polygenic, and total EBV of the full data set and the reduced data set.
2SCS = lactation-average SCS; CM1 = clinical mastitis between d −15 and 50; CM2 = clinical mastitis between d 51 and 300.
is memory intensive. To limit memory, IBD matrices were constructed using a 1-dimensional array and an efficient search algorithm to limit computing time. Second, convergence of the marker-assisted breeding value estimation with an IBD matrix was slow. This was due to the model having 5 very similar matrices for the ungenotyped cows, leading to high correlations between effects and thus resulting in slow convergence. Furthermore, many more effects need to be estimated with IBD haplotypes than with IBS haplotypes, which may lead to the lower accuracy of the total EBV than with IBS haplotypes. Therefore, using IBS haplotypes seems to be much more robust and practically feasible to implement in large populations.

**CONCLUSIONS**

In this study, we showed that marker-assisted breeding value estimation using IBD or IBS haplotypes is feasible even for large populations. The 5 QTL explained only a small proportion of genetic variance, especially with IBS haplotypes. The estimated QTL variances when using IBD haplotypes might have been inflated by capturing family-specific effects. The use of IBD haplotypes gave more reranking of bulls and cows than use of IBS haplotypes. Cross-validation showed no increase in predictive ability when using IBS haplotypes compared with conventional breeding value estimation, whereas a decrease in predictive ability was observed with IBD haplotypes. Furthermore, computing time was lower and convergence was better with IBS haplotypes than with IBD haplotypes. For mastitis resistance evaluation in Finnish Ayrshire, conventional breeding value estimation would be advocated because of the lack in improvement of accuracy and predictive ability when using marker-assisted breeding value estimation. However, it is expected that in situations where IBS haplotypes would explain 10 to 20% of the genetic variance, marker-assisted breeding value estimation with IBS haplotype may yield higher accuracy and predictive ability than conventional breeding value estimation.

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**REFERENCES**


